The following report contains NCCN Flash Updates™ relative to the first quarter of 2018, listed in chronological order with the most recent updates first.

March 30, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Breast Cancer. These NCCN Guidelines® are currently available as Version 1.2018.

- Recurrent/Stage IV (M1) Disease (BINV-17)
  - Added “For patients with HER2-negative tumors eligible for single-agent therapy, strongly consider germline BRCA 1/2 testing” to the workup.

- Systemic Treatment of Recurrent or Stage IV (M1) Disease, ER and/or PR-Positive; HER2 Negative
  - No prior endocrine therapy within 1 year, postmenopausal added “CDK4/6 inhibitor + aromatase inhibitor (category 1)” and removed “Palbociclib + aromatase inhibitor (category 1) or Ribociclib + aromatase inhibitor (category 1).” (BINV-20)
  - Footnote “iii” is new: “The potential side effects of additional chemotherapy may outweigh any clinical benefit in a patient who has a compromised performance status.” (BINV-21, -24, -25 and -26)

- Preoperative/Adjuvant Therapy Regimens (BINV-K)
  - Categorized therapy regimens as: “preferred regimens”, “other recommended regimens”, and regimens “useful in certain circumstances”.
  - Footnote “7” is new: “It would be acceptable to change the administration sequence to paclitaxel followed by dose-dense AC.”

- Systemic Therapy for ER and/or PR-Positive Recurrent or Stage IV (M1) Disease (BINV-N)
  - Categorized therapy regimens as: “preferred regimens”, “other recommended regimens”, and regimens “useful in certain circumstances”.
  - Added: Abemaciclib + aromatase inhibitor (category 1) as a preferred regimen option.
  - Modified footnote 3 by replacing “palbociclib or ribociclib” with “CDK4/6 inhibitor.”
  - Added: Ribociclib + tamoxifen (category 1) as a preferred regimen option.
    - Footnote “7” is new: “May be considered as a treatment option for first-line therapy with ovarian suppression or ablation for premenopausal patients with hormone-receptor positive, HER2-negative metastatic breast cancer.”

- Chemotherapy Regimens for Recurrent or Stage IV (M1) Disease (BINV-O)
  - Categorized therapy regimens as: “preferred regimens”, “other recommended regimens”, and regimens “useful in certain circumstances”.
  - Clarified olaparib recommendation by adding: “(option for patients with HER2-negative tumors and germline BRCA 1/2 mutation).”
  - Removed the following combination regimens:
    - CAF/FAC (cyclophosphamide/doxorubicin/fluorouracil)
    - FEC (fluorouracil/epirubicin/cyclophosphamide)
  - Modified footnote “2”: “There is no compelling evidence that combination regimens are superior to sequential single agents.” “Sequential single agents are preferred, but chemotherapy combinations may be used in select patients with high tumor burden, rapidly progressing disease, and visceral crisis.”

The following NCCN Chemotherapy Order Templates (NCCN Templates®) have been deleted to reflect the NCCN Guidelines for Breast Cancer Version 1.2018.

- Recurrent or Metastatic Human Epidermal Growth Factor Receptor 2 (HER2)-positive
  - BRS1: FAC (Fluorouracil/DOXOrubicin/IV Cyclophosphamide)
  - BRS2: CAF (Oral Cyclophosphamide/DOXOrubicin/Fluorouracil)
  - BRS3: CEF (Oral Cyclophosphamide/EpiRUBicin/Fluorouracil)
  - BRS40: FEC (Fluorouracil/EpiRUBicin/IV Cyclophosphamide)

March 29, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Central Nervous System Cancers. These NCCN Guidelines® are currently available as Version 1.2018.

- Title modified to include: Adult Low-Grade (WHO Grade II) Infiltrative Supratentorial Astrocytoma/Oligodendroglioma (Excluding Pilocytic Astrocytoma) (ASTRA-1 and ASTR-2)
  - For patients with MRI compatible with a low-grade glioma, removed “Observation” as an alternative to surgery, and removed the corresponding footnote: “Surgery is generally recommended, but serial observations are appropriate for selected patients.” (ASTRA-1)
  - Footnote “f” was modified to include: “Recommended molecular diagnostics include 1p19q chromosomal status and IDH1/2 mutation status, See Principles of Brain Tumor Pathology (BRAIN-F).” (ASTRA-1 and ASTR-2).
  - Footnote “i”, defining “high risk”, was modified to include: “Other high-risk factors that are sometimes taken into consideration are tumor size, neurologic deficits and presence of sequencing verified IDH wild type.” (ASTRA-1)
  - Adjuvant Treatment (ASTRA-1)
    - “Fractionated external beam RT (category 2B) or Chemotherapy (category 2B)” has been deleted from the pathway for low risk patients and included in the following footnote: “In the event that other risk factors are considered and treatment is warranted, treat as high-risk; there are potential unique circumstances in which fractionated external beam RT alone (category 2B) or chemotherapy alone (category 2B) may be considered.”

- Anaplastic Gliomas/Glioblastoma
  - Footnotes (GLIO-1)
    - The option for carmustine (BCNU) wafer implant during maximal safe resection (category 2B) has been deleted from the pathway and incorporated into a footnote.
  - Adjuvant Treatment (GLIO-2)
    - For “Anaplastic astrocytoma, Anaplastic oligoastrocytoma, NOS”, “Fractionated external beam RT” was removed as an option, and the following option was added: “Fractionated external beam RT followed by adjuvant temozolomide”
    - For “Anaplastic gliomas poor performance status (KPS <60)”, PCV was removed as a treatment option, and the following footnote was added to the “Temozolomide (category 2B)” option: “Consider temozolomide if tumor is MGMT promoter methylated (category 2B)” (GLIO-2A)
  - Adjuvant Treatment for Newly Diagnosed Glioblastoma (GLIO-3 and GLIO-4)
For patients of any age with good performance status (KPS ≥60), and any MGMT promoter status, the following treatment option was changed from category 2A to category 1 (GLIO-3 and GLIO-4): “Standard brain RT + concurrent temozolomide and adjuvant temozolomide + alternating electric field therapy”

For patients with age ≥70 y and poor performance status (KPS <60), “Standard Brain RT” was removed as an option, and the following option was amended: “Hypofractionated RT (preferred) ± concurrent or adjuvant TMZ” (GLIO-3)

For patients with age >70 y and good performance status (KPS ≥60), with any MGMT promoter status, the following option was changed from category 1 to category 2A: “Hypofractionated brain RT alone” (GLIO-4)

For patients with age >70 y and good performance status (KPS ≥60), “Hypofractionated brain RT + concurrent and adjuvant temozolomide” was added as an option for patients with MGMT promoter status unmethylated or indeterminate, and was changed from a category 2A to a category 1 designation for patients with MGMT promoter methylation. (GLIO-4)

For local resectable recurrent disease, the option for carmustine (BCNU) wafer implant during resection has been deleted from the pathway and incorporated into a footnote. (GLIO-5 and GLIO-5A)

Adult Medulloblastoma

- Molecular analysis was added as a component of postoperative staging, along with a new footnote: “Molecular profiling to identify clinically relevant subtypes is recommended to encourage opportunities for clinical trial involvement. See Principles of Pathology (BRAIN-F)”. (AMED-2)

Primary CNS Lymphoma

- Treatment for Relapsed or Refractory Primary CNS Lymphoma (PCNS-3)
  - 1st treatment option for patients with, “Prior high-dose methotrexate-based regimen without prior RT”, “Previous response with long duration (>12 mo)”, modified: “Re-treat with high-dose methotrexate ± other chemotherapy”.

Meningiomas

- This page has been extensively revised (MENI-1)

Limited Brain Metastases

- Title modified: “Limited (1-3) Extensive Brain Metastases”, and footnote "c" added on LTD-1 and LTD-3: “Limited brain metastases defines a group of patients for whom SRS is equally effective and offers significant cognitive protection compared with WBRT. The definition of ‘limited’ brain metastases in terms of number of metastases or total intracranial disease volume is evolving and may depend on the specific clinical situation...”

- LTD-1 and LTD-2 have been extensively revised.

Extensive Brain Metastases

- The title of this section has been revised, “Multiple (>3) Extensive Brain Metastases.”

- MU-1 has been extensively revised.

Principles of Brain and Spinal Cord Tumor Radiation Therapy (BRAIN-C)

- Low-Grade Gliomas (Grades I/II), sentence added to first bullet: “Consider RT dose escalation to 59.4–60 Gy for IDH-wildtype low-grade gliomas, as these patients may have a more aggressive course of disease.” (BRAIN-C 1 of 4)

- Ependymoma, sentence added to second bullet: “To reduce toxicity from craniospinal irradiation in adults, consider the use of intensity-modulated radiotherapy or protons if available.” (BRAIN-C 1 of 4)

- Brain Metastases, sentence added to first bullet: “For better prognosis patients consider memantine during and after WBRT for a total of 6 months.” (BRAIN-C 3 of 4)
Metastatic Spine, second bullet added: “Stereotactic radiation approaches (SRS/SBRT) for spinal cases may be preferred for patients with oligometastatic disease where tumor ablation is a goal of treatment and in tumors considered radioresistant (eg, renal cell, melanoma, sarcoma, hepatocellular, and some colorectal and NSCLC cases). Stereotactic radiation may also be preferred in the setting of tumor recurrence after prior radiation as a strategy to limit radiation dose to the spinal cord or other critical structures. Careful adherence to consensus guidelines for radiosurgery planning and delivery is recommended.” (BRAIN-C 3 of 4)

- Principles of Brain and Spinal Cord Tumor Systemic Therapy
  - Anaplastic Gliomas (BRAIN-D 1 of 8)
    - Adjuvant Treatment
      - List of options revised to match GLIO-2
      - For “Anaplastic astrocytoma/anaplastic oligoastrocytoma, NOS (KPS ≥60)” defined the temozolomide regimen in the following new treatment option: “RT followed by adjuvant TMZ (12 cycles)”
  - Meningiomas (BRAIN-D 2 of 8)
    - Added new option: “Bevacizumab + everolimus (category 2B)”
  - Primary CNS Lymphomas (BRAIN-D 3 of 8)
    - “Induction Therapy”, was modified as follows:
      - “Systemic Therapy” sub-header added, with the following options revised as shown:
        - High-dose methotrexate 8 g/m² combined with the following plus deferred RT:
          - Rituximab
          - Rituximab and temozolomide
        - High-dose methotrexate 3.5 g/m² combined with the following, and consider WBRT plus RT:
          - Vincristine, procarbazine, cytarabine ± and rituximab (R-MPV)
          - Temozolomide + rituximab followed by post RT temozolomide
          - Cytarabine
          - Ifosfamide ± RT
    - “Consider urgent glucarpidase (carboxypeptidase G2) for prolonged methotrexate clearance due to methotrexate-induced renal toxicity”, is now a footnote wherever systemic methotrexate is recommended
    - “Intra-CSF therapy” was added, with the following options:
      - Methotrexate
      - Cytarabine
      - Rituximab
    - “Consolidation Therapy” options were modified as follows:
      - High-dose chemotherapy with stem cell rescue
        - Carmustine + thiopeta
        - Thiotepa, busulfan, and cyclophosphamide (TBC)
      - High-dose cytarabine ± etoposide (EA)
      - High-dose cytarabine
    - “Recurrence or Progressive Disease” revised to “Relapsed or Refractory Disease”, and some of the options listed modified as follows:
      - Retreat with high-dose methotrexate with or without rituximab
      - Ibrutinib
• Lenalidomide with or without rituximab
• Consider high-dose chemotherapy with autologous stem cell reinfusion in eligible patients who achieve a CR with conventional doses of chemotherapy
  o Brain Metastases (BRAIN-D 4 of 8)
    ▪ “Newly Diagnosed” section is new, with the following options:
      • BRAF/MEK inhibitor combination (melanoma):
        o Vemurafenib/cobimetinib
        o Dabrafenib/trametinib
      • Ipilimumab + nivolumab (melanoma)
      • Pembrolizumab (melanoma or non-small cell lung cancer)
      • Alectinib (ALK rearrangement-positive NSCLC)
    ▪ Recurrent Disease, new options added:
      • Capecitabine + neratinib (breast)
      • Paclitaxel + neratinib (breast) (category 2B)
      • BRAF/MEK inhibitor combination therapy (melanoma):
        o Vemurafenib/cobimetinib
        o Dabrafenib/trametinib
      • Ceritinib, alectinib, brigatinib (ALK rearrangement-positive NSCLC)
    ▪ Leptomeningeal Metastases
      • Intra-CSF chemotherapy, the following change was made:
        o Liposomal cytarabine (lymphoma/leukemias)
• Principles of Brain and Spine Tumor Management
  ▪ This section of the guidelines has been extensively revised (BRAIN-E)
• Principles of Brain Tumor Pathology
  ▪ This section of the guidelines has been extensively revised, and new sections added: ATRX Mutation, TERT Mutation, H3F3A Mutation, BRAF Mutation, RELA Fusion, Medulloblastoma Molecular Subtyping (BRAIN-F)

Previous updates to the NCCN Guidelines for Central Nervous System Cancers can be found in the UPDATES section of the current version.

NCCN has published updates to the NCCN Guidelines for Soft Tissue Sarcoma. These NCCN Guidelines are currently available as Version 2.2018.

• The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

Previous updates to the NCCN Guidelines for Soft Tissue Sarcoma can be found in the UPDATES section of the current version.
NCCN has published updates to the NCCN Guidelines for Bone Cancer. These NCCN Guidelines are currently available as Version 2.2018.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

Previous updates to the NCCN Guidelines for Bone Cancer can be found in the UPDATES section of the current version.

March 27, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colorectal Cancer Screening. These NCCN Guidelines® are currently available as Version 1.2018.

- Average Risk Screening
  - Under Screening Modality and Schedule,
    - Flexible sigmoidoscopy was revised by removing, “± interval high-sensitivity guaiac-based or immunochemical-based testing at year 3” and the subsequent algorithm related to stool testing results was removed. (CSCR-3)
    - CT colonography (CTC), after negative/no polyps, the evaluation was revised as, “Rescreen with any modality in 5 y.” (CSCR-3)
    - Footnote “h” was added: “Based on recent evidence, FIT has been shown to have superior sensitivity to guaiac-based tests. However, guaiac-based testing has been shown to reduce mortality from CRC and high-sensitivity FOBT is a reasonable alternative if an immunochemical test cannot be used. (Rabeneck L, et al. Can J Gastroenterol 2012;26:131-147; Scholefield JH, et al. Gut 2012;61:1036-1040.)” (CSCR-2)
    - Footnote “m” was added, “There are alternative strategies that have been recommended with flexible sigmoidoscopy, including flexible sigmoidoscopy every 10 years with annual FIT or considering longer interval flexible sigmoidoscopy without FIT (Knudsen A, Zauber A, Rutter C, et al. Estimation of benefits, burden, and harms of colorectal cancer screening strategies: Modeling study for the US Preventive Services Task Force. JAMA 2016;315:2595-2609).” (CSCR-3)
  - Personal History of Adenomatous Polyp or Sessile Serrated Polyp (CSCR-4)
    - Clinical Findings
      - SSP without dysplasia was separated out from low-risk polyps into “intermediate-risk polyps.”
    - Follow-up of Clinical Findings
      - Low-risk polyps was changed from “repeat colonoscopy within 5–10 y” to “Repeat colonoscopy between 5–10 y.”
      - Intermediate risk follow-up was added, “Repeat colonoscopy in 5 y.”
      - High risk was changed from “Repeat colonoscopy within 3 y” to “Repeat colonoscopy in 3 y.”
        - The follow-up for “negative for adenoma or SSP ± low risk polyps” was revised from “Repeat colonoscopy within 5 y” to “Repeat colonoscopy in 5 y.”
        - The follow-up for positive/adenoma or SSP was changed to “Repeat colonoscopy according to clinical findings” rather than looping back to the beginning of the algorithm.
• Increased Risk Based on Personal History of Colorectal Cancer (CSCR-5)
  ▪ Footnote “r” was revised, “The panel recommends universal screening of all CRC tumors to maximize
  sensitivity for identifying individuals with LS, and to simplify inform prognosis and care processes in
  patients with and without LS. However, evidence suggests an alternate option would be to limit
  screening to individuals with CRC diagnosed <70 y plus those >70 y meeting Bethesda guidelines.
  The panel recommends tumor testing with IHC and/or MSI be used as the primary approach for
  pathology lab–based universal screening and to guide treatment decisions.”

• Increased Risk Based on Personal History of Inflammatory Bowel Disease (CSCR-6)
  ▪ Under Surveillance Modality and Schedule,
    ▪ Colonoscopy, the 1st sub-bullet for HD-WLS/SD-WLE was revised, “Random 4 quadrant biopsies
      every 10 cm with >33 32 total samples.”

• Increased Risk Based on Positive Family History (CSCR-8)
  ▪ Screening, footnote “ff” was added, “For individuals not willing to undergo colonoscopy, there are
    emerging data that FIT may be a reasonable substitute.”

• Screening Modality and Schedule (CSCR-A 4 of 5)
  ▪ CTC, 1st bullet, 2nd sub-bullet was revised, Lesions 5 6 –9 mm can be identified with an acceptable
    accuracy that is less than that identified for colonoscopy.”

NCCN has published updates to the NCCN Guidelines for Penile Cancer. These NCCN Guidelines are
currently available as Version 2.2018.

• The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

Previous updates to the NCCN Guidelines for Penile Cancer can be found in the UPDATES section of the current
version.

NCCN has published updates to the NCCN Guidelines for Chronic Lymphocytic Leukemia/Small
Lymphocytic Lymphoma. These NCCN Guidelines are currently available as Version 5.2018.

• The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

Previous updates to the NCCN Guidelines for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma can
be found in the UPDATES section of the current version.

NCCN has published updates to the NCCN Guidelines and NCCN Drugs & Biologics Compendium (NCCN
Compendium®) for Cancer-Associated Venous Thromboembolic Disease. These NCCN Guidelines and are
currently available as Version 1.2018.

• “Workup and Management of Suspected HIT” page was extensively revised. (HIT-1)
• “Treatment of HIT” page was extensively revised. (HIT-2)
• The pages for therapeutic anticoagulation for venous thromboembolism were extensively revised and reorganized. (VTE-E)
• Reversal of Anticoagulation in the Event of Life-Threatening Bleeding or Emergent Surgery (VTE-F 6 of 9)
  ° 4th sub-bullet for reversal of argatroban was added: “Monitor reversal for aPPT”
  ° 5th bullet for reversal of dabigatran was added: “Monitor reversal with aPPT or dilute TT or Hemoclot thrombin inhibitor test to ensure complete reversal”
• Contraindications to Thrombolysis (VTE-J)
  ° Platelet count was removed from the list of absolute contraindications.

NCCN has updated the NCCN Radiation Therapy Compendium™ to reflect recommendations within the following NCCN Guidelines:

• Acute Lymphoblastic Leukemia (ALL) version 1.2018
• Esophageal and Esophagogastric Junction Cancers version 1.2018
• Gastric Cancer version 1.2018
• Head and Neck Cancers version 1.2018
• Rectal Cancer version 1.2018

NCCN has added a NEW disease site to the NCCN Radiation Therapy Compendium™ to reflect recommendations within the following NCCN Guidelines:

• Uveal Melanoma version 1.2018

March 16, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Esophageal and Esophagogastric Junction Cancers. These NCCN Guidelines® are currently available as Version 1.2018.

• Workup (ESOPH-1)
  o Fifth bullet revised, “PET/CT evaluation (skull base to mid-thigh) if no evidence of M1 disease.”
• Adenocarcinomas
  o Primary Treatment Options for Medically Fit Patients: For Stage cT4b tumors, the following option was added, “Consider chemotherapy alone in the setting of invasion of trachea, great vessels, or heart. See Palliative Management.” (ESOPH-13)
  o Postoperative Management for R1 Resection Patients Who Received Preoperative Chemoradiation or Chemotherapy (ESOPH-16)
    • “Observation until progression” added as an option.
    • “Chemotherapy if received preoperatively” removed as an option.
• Principles of Pathologic Review and Biomarker Testing (ESOPH-B)
  o Section title revised, “Principles of Pathologic Review and HER2 Biomarker Testing.”
  o This section was extensively revised and includes new recommendations for “Microsatellite Instability (MSI) or Mismatch Repair (MMR) Testing” and “PD-L1 Testing.”
• Principles of Systemic Therapy (ESOPH-F)
  o Perioperative Chemotherapy revisions
    • “Fluoropyrimidine and oxaliplatin” changed to a preferred option.
“Fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) (category 1)” added as an option with corresponding footnote, “Due to toxicity, three-drug regimens are recommended only in select patients who are medically fit.”

The following regimens were removed:

- ECF (epirubicin, cisplatin, and fluorouracil) (category 2B)
- ECF modifications (category 2B for all modifications)
  - Epirubicin, oxaliplatin, and fluorouracil
  - Epirubicin, cisplatin, and capecitabine
  - Epirubicin, oxaliplatin, and capecitabine

Principles of Surveillance (ESOPH-I)

- First bullet of the introductory page revised: “The surveillance strategies after successful local therapy for esophageal and EGJ cancers remain controversial, with little prospective data to construct appropriate algorithms that balance the benefits and risks (including cost) within a population. No high-level evidence to guide development of algorithms that balance benefits and risks (including cost) within this cohort.”
- For patients with T1b, Any N tumors who had esophagectomy, revised recommendation, “Imaging (CT chest/abdomen with contrast unless contraindicated) can be considered starting at 6–12 months and every 12 months for up to 3 years then as clinically indicated if the patient is likely to tolerate additional curative-intent therapy for recurrence. EGD as needed…”
- For patients with T2-T4, N0-N+, T4b tumors who received bimodality therapy (definitive chemoradiation), revised recommendation, “Imaging studies (CT chest/abdomen with contrast unless contraindicated) are recommended should be considered every 6 months for up to 2 years if the patient is likely to tolerate additional curative-intent therapy for recurrence. Frequency may be every 4–6 months in the first 12 months and then less frequently in the next 24 months. EGD every…”
- For patients with T2-T4, N0-N+, T4b tumors who had trimodality therapy, revised, “Imaging studies (CT chest/abdomen with contrast unless contraindicated) are recommended should be considered every 6 months for up to 2 years if the patient is likely to tolerate additional curative-intent therapy for recurrence. Frequency of surveillance may be every 4–6 months in the first 12 months and every 6–9 months in the next 24 months. Unscheduled…”

Staging (ST-1)

- The AJCC 7th Edition Cancer Staging Tables were updated to the 8th edition.

NCCN has published updates to the NCCN Guidelines and the NCCN Compendium for Gastric Cancer. These NCCN Guidelines are currently available as Version 1.2018.

Workup (GAST-1)

- Fourth bullet revised: “PET/CT evaluation (skull base to mid-thigh) if no evidence of M1 disease and if clinically indicated.”
- Sixth bullet revised: “Endoscopic ultrasound (EUS) if no evidence of M1 disease early stage disease suspected or if early versus locally advanced disease needs to be determined (preferred).”

Primary Treatment (GAST-2)

- Medically fit, potentially resectable patients with tumors staged cT2 or higher, Any N
  - "Perioperative chemotherapy (category 1)" changed to a preferred recommendation.
  - After perioperative chemotherapy and preoperative chemoradiation, a new "Response Assessment" pathway (GAST-3) was added. Previously surgery was recommended for these patients.
- Surgically unresectable: Systemic therapy added as an option.
• Postoperative Management for Patients Who Have Not Received Preoperative Chemotherapy or Chemoradiation (GAST-4)
  o For R0 resection patients staged pT3, pT4, Any N or Any pT, N+:
    ▪ Revised, “Fluoropyrimidine (fluorouracil or capecitabine), then fluoropyrimidine-based chemoradiation, then fluoropyrimidine (fluorouracil or capecitabine), if less than a D2 dissection (category 1).”
    ▪ Revised, “Chemotherapy for patients who have undergone primary D2 lymph node dissection” changed from category 2A to category 1.

• Palliative Management (GAST-9)
  o Karnofsky performance score ≥60% or ECOG performance score ≤2": “Chemoradiation (only if locally unresectable and not previously received)” added as an option.

• Principles of Pathologic Review and Biomarker Testing GAST-B)
  o Section title revised, “Principles of Pathologic Review and HER2 Biomarker Testing.”
  o This section was extensively revised and includes new recommendations for “Microsatellite Instability (MSI) or Mismatch Repair (MMR) Testing” and “PD-L1 Testing.”

• Principles of Genetic Risk Assessment (GAST-D)
  o Surveillance recommendations
    ▪ Hereditary diffuse gastric cancer: Recommendation revised, “Prophylactic total gastrectomy is recommended between ages 18 and 40 for CDH1 mutation carriers. A baseline endoscopy with multiple random biopsies is indicated prior to prophylactic total gastrectomy. Intraoperative frozen sections should be...”
    ▪ Lynch syndrome (LS): Recommendation revised, “Selected individuals or families or those of Asian descent may consider EGD with extended duodenoscopy (to distal duodenum or into the jejunum). Given the lower expected risk of gastric cancer in MSH6 and PMS2 mutation carriers, gastric cancer screening recommendations are for MLH1, MSH2, and EPCAM mutation carriers at this time. See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal for additional screening recommendations.”

• Principles of Systemic Therapy (GAST-F)
  o Perioperative Chemotherapy revisions
    ▪ “Fluoropyrimidine and oxaliplatin” changed to a preferred option.
    ▪ “Fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) (category 1)” added as an option with corresponding footnote, “Due to toxicity, three-drug regimens are recommended only in select patients who are medically fit.”
  o The following regimens were removed:
    • ECF (epirubicin, cisplatin, and fluorouracil) (category 2B)
    • ECF modifications (category 2B for all modifications)
      o Epirubicin, oxaliplatin, and fluorouracil
      o Epirubicin, cisplatin, and capecitabine
      o Epirubicin, oxaliplatin, and capecitabine

• Staging (ST-1)

The AJCC 7th Edition Cancer Staging Tables were updated to the 8th edition.
March 15, 2018

NCCN has published NEW NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Uveal Melanoma. The NCCN Guidelines® and NCCN Compendium® are currently available as Version 1.2018.

- The new NCCN Guidelines cover the full continuum of care for all stages of uveal melanoma arising in the choroid or ciliary body, including potentially pre-cancerous nevi and distant metastatic disease.

NCCN has published updates to the NCCN Chemotherapy Order Templates (NCCN Templates®) for Non-Small Cell Lung Cancer to reflect the currently published NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer Version 3.2018.

- The following information has been updated for NSC61 – Ceritinib
  - Dosing of ceritinib has changed from 750 mg to 450 mg to reflect current FDA-approved dosing
  - The following note has been updated in the Safety Parameters and Special Instructions section: “Take with food”
    - previously “Take on an empty stomach”

March 14, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis. These NCCN Guidelines® are currently available as Version 1.2018.

- Principles of Emesis Control for the Cancer Patient (AE-1)
  - Added a new bullet: While chemotherapy or radiation therapy-induced nausea and vomiting can significantly impact a patient’s quality of life and lead to poor outcomes, providers must be aware of the potential for the overuse of prophylactic antiemetics, especially for chemotherapy with minimal and low emetic risks, which may expose the patient to potential adverse effects from antiemetic drugs and pose an undue economic burden. Guideline adherence is always encouraged. Okuyama A, Nakamura F, Higashi T. Prescription of prophylactic antiemetic drugs for patients receiving chemotherapy with minimal and low emetic risk. *JAMA Oncol*. 2017;3(3):344-350. Encinosa W, Davidoff AJ. Changes in antiemetic overuse in response to Choosing Wisely recommendations. *JAMA Oncol*. 2017;3(3):320–326.

- Emetogenic Potential of Intravenous Anticancer Agents
  - Moderate emetic risk (AE-2), added: Dual-drug liposomal encapsulation of cytarabine/daunorubicin.
  - Low emetic risk (AE-3), added: Olaratumab.
  - Minimal emetic risk (AE-3), added: Avelumab and rituximab/hyaluronidase human injection for SQ use.

- Emetogenic Potential of Oral Anticancer Agents
  - Moderate to high emetic risk (AE-4), added: Enasidenib, midostaurin, and niraparib.
  - Minimal to low emetic risk (AE-4), added: Abemaciclib, brigatinib, neratinib, and ribociclib.

- High Emetic Risk Intravenous Chemotherapy – Acute and Delayed Emesis Prevention (AE-5) and Moderate Emetic Risk Intravenous Chemotherapy – Acute and Delayed Emesis Prevention (AE-6)
NCCN Flash Updates™

1st Quarter 2018

- These pages were extensively reformatted.
- New NK-1RA option for Day 1: Aprepitant injectable emulsion 130 mg IV once.
- New NK-1RA option for Day 1: Rolapitant 166.5 mg IV once.
- Day 1, changed dose of dexamethasone from 20 mg IV to 12 mg PO/IV once.

- Revised and reformatted the footnotes to correspond with changes made on AE-5 and AE-6. (AE-7)
  - Footnote “k” is new: Aprepitant injectable emulsion is a unique formulation of aprepitant and is NOT interchangeable with the intravenous formulation of fosaprepitant.
  - Footnote “n” is new: If netupitant/palonosetron fixed combination product is used, no further 5-HT 3RA is required.

- Breakthrough Treatment for Chemotherapy-Induced Nausea/Vomiting (AE-10)
  - Dronabinol 5-10 mg PO every 4-6 h was changed to 3-4 times daily.
  - Footnote bb is new: Dronabinol oral solution has greater oral bioavailability than dronabinol capsules. 2.1 mg oral solution = 2.5 mg capsules. Dronabinol capsules 5-10 mg PO or dronabinol oral solution 2.1-4.2 mg/m² PO, given three-four times daily.

- Anticipatory Emesis Prevention/Treatment (AE-12)
  - Added the following behavioral therapy: Progressive muscle relaxation, Biofeedback, Cognitive distraction, and Yoga (if approved by physician).
  - Consider anxiolytic therapy, removed the example of alprazolam from 0.5-1 mg.

- Principles of Managing Multiday Emetogenic Chemotherapy Regimens (AE-A)
  - Added: If patients cannot tolerate dexamethasone, consider replacing with olanzapine.
  - Added: aprepitant injectable emulsion to NK1 section.

- Pharmacologic Considerations for Antiemetic Prescribing (AE-B)
  - Benzodiazepines
    - Added: Parenteral olanzapine use with concomitant parenteral benzodiazepine use is contraindicated
    - Added: Use with caution in patients with scheduled opioids.

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Colon Cancer and Rectal Cancer. These NCCN Guidelines for Colon Cancer® are currently available as Version 2.2018. The NCCN Guidelines for Rectal Cancer® are currently available as 1.2018.

- Workup (COL-2)
  - Bullet 4 added: Consider abdominal/pelvic MRI
  - Footnote j added: Consider an MRI to assist with the diagnosis of rectal cancer versus colon cancer (e.g. low lying sigmoid tumor). The rectum lies below a virtual line from the sacral promontory to the upper edge of the symphysis as determined by MRI.

- Workup (REC-2)
  - Bullet 4 added: Consider rigid proctoscopy
  - Bullet 5 modified: Chest CT and abdominal/pelvic CT or MRI
  - Bullet 7 modified: Pelvic MRI with contrast (preferred)
  - Bullet 8 clarified: Endorectal ultrasound (only if MRI is contraindicated [e.g. pacemaker])
  - Footnote j added: For optimizing care of older adult patients with cancer, see the NCCN Guidelines for Older Adult Oncology.
  - Footnote j added: The rectum lies below a virtual line from the sacral promontory to the upper edge of the symphysis as determined by MRI.

- Clinical stage (REC-2)
T3-4, N0 or T any, N1-2 replaced with the following

- T3, N any with clear circumferential margin (CRM) (by MRI); T1-2, N1-2
  - Footnote l added: CRM measured at the closest distance of the tumor to the mesorectal fascia. Clear CRM: Greater than 1 mm from mesorectal fascia, levator muscles and not invading into the intersphincteric plane.
- T3, N any with involved CRM (by MRI); T4, N any
  - Footnote m added: CRM measured at the closest distance of the tumor to the mesorectal fascia. Involved CRM: within 1 mm of mesorectal fascia; or, for lower third rectal tumors, within 1 mm from levator muscle; or, for anal canal lesions, invasion into or beyond the intersphincteric plane.

Pathologic Findings after Transanal Local Excision for T1, N0 (REC-3)

- pT1, NX with high-risk features or pT2, NX
  - Transabdominal resection noted as preferred for pT2 lesions
  - Transabdominal resection: pT3, N0, M0 pulled out as own category to exclude oxaliplatin-based treatment options. Options include infusional 5-FU/RT (preferred) or capecitabine/RT (preferred) or bolus 5-FU/leucovorin/RT followed by 5-FU/leucovorin (infusional preferred) or capecitabine OR observation in select patients. (also applies to REC-4)
  - Treatment option modified after Chemo/RT: Consider observation (if complete response no evidence of disease)

- Footnote r added: Observation following transabdominal resection can be considered in patients with pT3N0 rectal cancer if the tumor was well-differentiated or moderately well-differentiated carcinoma invading less than 2 mm into the mesorectum, without lymphatic or venous vessel involvement and was located in upper rectum. Willett CG, Badizadegan K, Ancukiewicz M, Shellito PC. Prognostic factors in stage T3N0 rectal cancer: do all patients require postoperative pelvic irradiation and chemotherapy? Dis Colon Rectum 1999;42:167-173. (also applies to REC-4)

Clinical Stage: T3, N any with clear circumferential margin (CRM) (by MRI); T1-2, N1-2 (REC-5)

- Short-course RT added as a treatment option after neoadjuvant chemotherapy
- Primary Treatment
  - Restaging added after primary treatment with chemotherapy followed by chemo/RT or short-course RT
  - Chemo/RT followed by transabdominal resection
    - Added: “Consider restaging” before resection
    - Adjuvant treatment modified based on clinical staging before chemo/RT
      - cT3, N0: 5-FU/leucovorin or capecitabine or FOLFOX (preferred) or CAPEOX (preferred)
      - cT1-3, N1-2: FOLFOX or CAPEOX
  - Footnote u added: If patient treated with short course RT, surgery should be within 1 week or delayed 6-8 weeks. (also applies to REC-8, REC-9)
  - Footnote v added: In those patients who achieve a complete clinical response with no evidence of residual disease on digital rectal examination, rectal MRI, and direct endoscopic evaluation, a “watch and wait,” nonoperative management approach may be considered in centers with experienced multidisciplinary teams. The degree to which risk of local and/or distant failure may be increased relative to standard surgical resection has not yet been adequately characterized. Decisions for nonoperative management should involve a careful discussion with the patient of his/her risk tolerance. (also applies to REC-6)

Clinical Stage: T3, N any with involved CRM (by MRI); T4, N any or Locally unresectable or medically inoperable (REC-6)

- Neoadjuvant Therapy
Short-course RT removed
Chemotherapy clarified as 12-16 weeks
  Restaging added after chemotherapy followed by chemo/RT
Chemo/RT
  Restaging added at 6 weeks post completion of RT
  Further treatment decisions based on involvement of CRM; bulky residual disease; or clear CRM
  Involved CRM or bulky disease
    Chemotherapy added as a treatment option for 12-16 weeks: FOLFOX/CAPEOX (preferred) or 5-FU/leucovorin or capecitabine
    Restaging added after chemotherapy
    Chemotherapy added after transabdominal resection: FOLFOX/CAPEOX (preferred) or 5-FU/leucovorin or capecitabine

Clinical Presentation: Suspected or proven metastatic synchronous adenocarcinoma (REC-7)
  New page added to address the workup of patients with suspected or proven metastatic synchronous adenocarcinoma
Resectable synchronous liver only and/or lung only metastases (REC-8)
  Recommendations revised.
  Footnote z added: If obstructing lesion, consider diversion. (also applies to REC-9)
  Footnote aa added: There are limited data regarding available treatment options.
Unresectable synchronous liver only and/or lung only metastases or medically inoperable (REC-9)
  Recommendations revised.
  Footnote cc added: There should be at least a 6-week interval between the last dose of bevacizumab and elective surgery, and re-initiation of bevacizumab should be delayed at least 6–8 weeks postoperatively. There is an increased risk of stroke and other arterial events, especially in those aged ≥65 years. The use of bevacizumab may interfere with wound healing.
New page addressing synchronous abdominal/peritoneal metastases (REC-10)
Surveillance (REC-11)
  New condition added: Transanal excision only
    Proctoscopy (with EUS or MRI with contrast) every 3–6 mo for the first 2 y, then every 6 mo for a total of 5 y
    Colonoscopy at 1 y
      If advanced adenoma, repeat in 1 y
      If no advanced adenoma, repeat in 3 y, then every 5 y
  Stage II-IV: Proctoscopy recommendation removed.
Isolated pelvic/anastomotic recurrence (REC-12)
  Potentially resectable
    Preoperative Chemo/RT noted as preferred, if not previously given
Principles of Imaging section added (REC-A)
Continuum of Care – Systemic Therapy for Advanced or Metastatic Disease (COL-D/REC-F) 9 of 10
  Regorafenib dosing modified and reference added: 160 mg PO daily days 1-21, 80 mg PO daily on days 1-7, then 120 mg PO daily on days 8-14, then 160 mg PO daily on days 15-21; Subsequent cycles: Regorafenib 160 mg PO daily on days 1-21
Principles of Survivorship (REC-G 1 of 2)
  Management of Late/Long-Term Sequelae from of Disease or Treatment
Bullet 1 added: “For issues related to distress, pain, neuropathy, fatigue, or sexual dysfunction, see NCCN Guidelines for Survivorship”

Bullet 2 modified: Chronic diarrhea or incontinence. Bowel function changes: chronic diarrhea, incontinence, stool frequency, urgency, cramping

Bullet 2, sub-bullet 2 added
- Management of an ostomy
  - Consider participation in an ostomy support group or coordination of care with a health care provider specializing in ostomy care (i.e. ostomy nurse)
  - Screen for distress around body changes (See NCCN Guidelines for Distress Management) and precautions around involvement with physical activity (see page SPA-A in the NCCN Guidelines for Survivorship)

Bullet 3; sub-bullet 2 added
- Consider referral to pain management specialist for refractory cases

Counseling Regarding Healthy Lifestyle and Wellness
- Bullet 1 added: “Undergo all age and gender-appropriate cancer and preventive health screenings as per national guidelines”
- Bullet 5 modified: “Consider low-dose daily aspirin 325 mg for secondary prevention.”
- Bullet 6 modified: “Eliminate or limit alcohol consumption, no more than 1 drink/day for women, and 2 drinks/day for men.”

Staging in the NCCN Guidelines for Rectal Cancer (ST-1)

NCCN has published updates to the NCCN Guidelines for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. These NCCN Guidelines are currently available as Version 4.2018.

- Special considerations for the use of small-molecule inhibitors (CSLL-F, 2 of 3)
  - Venetoclax, 2nd bullet was revised from, "A more rapid dose escalation can occur (over 1 wk) for seriously ill patients with hospitalization and close inpatient monitoring for TLS. (Jones J, Mato A, Wierda W, et al. Venetoclax for chronic lymphocytic leukaemia progressing after ibrutinib: an interim analysis of a multicentre, open-label, phase 2 trial. Lancet Oncol 2018;19:65-75.)" to “Initiation and accelerated escalation of venetoclax (20 mg to 400 mg over 3-weeks) with close inpatient TLS monitoring can be done in the subgroup of patients with high tumor burden and where there is concern for rapid disease progression on or following BTK-inhibitor therapy. For accelerated escalation, venetoclax is administered at 20 mg on Week (W)1/Day (D)1, 50 mg on W1/D2-3, 100 mg on W1/D4-7 (all inpatient), then outpatient unless concern for TLS, 200 mg on W2/D1-7, and 400 mg on W3/D1-continuous.† Additionally, continued BTK-inhibition concurrent with initiation and escalation of venetoclax with discontinuation of BTK-inhibitor when up to the venetoclax 400 mg daily dose can be considered. These agents can be given together safely.”

*Previous updates to the NCCN Guidelines for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma can be found in the UPDATES section of the current version.
NCCN has published updates to the NCCN Guidelines for Bladder Cancer. These NCCN Guidelines are currently available as Version 3.2018.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

*Previous updates to the NCCN Guidelines for Bladder Cancer can be found in the UPDATES section of the current version.

March 13, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer Early Detection. These NCCN Guidelines® are currently available as Version 1.2018.

- Baseline evaluation (PROSD-2)
  - Modified last bullet: “Family or personal history of high-risk germline mutations BRCA1/2.”
  - Modified last sentence in footnote “c”: “If there is a known or suspected cancer susceptibility gene, referral to a cancer genetics professional is recommended. BRCA1/2 pathogenic mutation carriers are associated with an increased risk of prostate cancer before age 65 years, and prostate cancer in men with germline BRCA2 mutations occurs earlier and is more likely to be associated with prostate cancer mortality. Information regarding BRCA 1/2 gene status germline mutations should be used as part of the discussion about prostate cancer screening.”
  - Modified footnote “e”: “Testing above the age of 75 years of age should be done with caution and only in very healthy men with little or no comorbidity to detect the small number of aggressive cancers that pose a significant risk if left undetected until signs or symptoms develop. Widespread screening in this population would substantially increase rates of over-detection and is not recommended. as a large proportion may harbor cancer that would be unlikely to affect their life expectancy, and screening in this population would substantially increase rates of over-detection. However, a clinically significant small number of men in this age group may present with high-risk cancers that pose a significant risk if left undetected until signs or symptoms develop. Very few men above the age of 75 years benefit from PSA testing.”

- Indications for biopsy (PROSD-3)
  - Modified bullet: “Consider percent free PSA, 4Kscore, or PHI” to “Consider biomarkers that improve the specificity of screening”

- Management of biopsy results (PROSD-4)
  - Atypia, suspicious for cancer and multifocal high-grade PIN (>2 sites):
    - Modified first bullet: “Consider serum or urine tests biomarkers that improve the specificity of screening and/or multiparametric MRI”
  - Benign and focal high-grade PIN:
    - Modified bullet: “Consider percent free PSA, 4Kscore, PHI, PCA3, or ConfirmDX biomarkers that improve the specificity of screening and/or multiparametric MRI and/or refined prostate biopsy techniques
    - Footnote “i” is new to the page: “Biomarkers that improve the specificity of detection are not, as yet, recommended as first-line screening tests. However, there may be some patients who meet PSA standards for consideration of prostate biopsy, but for whom the patient and/or the physician wish to further define the probability of high-grade cancer. A percent-free PSA <10%, PHI >35, or 4Kscore
(which provides an estimate of the probability of high-grade prostate cancer) are potentially informative in patients who have never undergone biopsy or after a negative biopsy; a PCA3 score >35 is potentially informative after a negative biopsy. The predictive value of the serum biomarkers discussed above has not been correlated.

March 12, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®), and the NCCN Imaging Appropriate Use Criteria (NCCN Imaging AUC™) for Waldenström’s Macroglobulinemia/ Lymphoplasmacytic Lymphoma. These NCCN Guidelines® are currently available as Version 1.2018.

- Primary treatment (WM/LPL-2)
  - “Consider rituximab for maintenance therapy” added footnote "l": “Only for those who responded to rituximab-containing regimens.”

- Waldenström’s Macroglobulinemia/ Lymphoplasmacytic Lymphoma Therapy (WM/LPL-B)
  - Listed the regimens as “Preferred Regimens” and “Other Recommended Regimens.” (applies to WM/LPL-B, 1 and 2 of 3) and “Useful in certain circumstances” (WM/LPL-B, 2 of 3)
  - Footnote 1 is new: “Pneumocystis jiroveci pneumonia (PJP) prophylaxis should be considered for patients receiving bendamustine/rituximab or fludarabine/cyclophosphamide/rituximab.” (applies to WM/LPL-B, 1 and 2 of 3)
  - Chlorambucil, thalidomide ± rituximab, and alemtuzumab have been removed from the list of recommended treatment regimens for WM (applies to WM/LPL-B, 1 and 2 of 3).

The following NCCN Chemotherapy Order Templates (NCCN Templates®) have been deleted to reflect the NCCN Guidelines for Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 1.2018.

- WAL5: Thalidomide
- WAL6: Thalidomide + Rituximab
- WAL7: Chlorambucil
- WAL16: Alemtuzumab

NCCN has published updates to the NCCN Guidelines and the NCCN Compendium® for Prostate Cancer. These NCCN Guidelines are currently available as Version 2.2018.

- Systemic Therapy for M0 Castration-Resistant Prostate Cancer (PROS-14)
  - Removed: “Clinical trial (preferred) from the algorithm because it is listed on the bottom of the page. “Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.”
  - Changed: Observation especially if PSADT ≥ 10 mo to Observation especially if PSADT >10 mo.
  - Added a new option: Apalutamide especially if PSADT ≤10 mo (category 1).
• **Principles of Androgen Deprivation Therapy (ADT) (PROS-F)**
  - **Modified:** Orchiectomy (for M1)
  - **Modified:** Apalutamide (for M0) has been added to the list of second-generation antiandrogens as a secondary hormone therapy option for CRPC.
  - **Footnote 1 is new:** Abiraterone plus prednisone should not be coadministered with an antiandrogen.
  - **Footnote 2 is new:** Abiraterone is not an option for use in combination with docetaxel.
  - **Modified the following bullet:** In the setting in which patients have no or minimal symptoms, administration of secondary hormonal therapy including addition of, or switching to, a different antiandrogen (flutamide, bicalutamide, nilutamide, enzalutamide [M1 only], apalutamide [M0 only]), addition of adrenal/paracrine androgen synthesis inhibitors (ketoconazole with or without hydrocortisone or abiraterone with prednisone [M1 only]), or use of an estrogen, such as DES, can be considered. Ketoconazole ± hydrocortisone should not be used if the disease progressed on abiraterone. (PROS-F, 3 of 4)
  - **Added a new bullet:** “A phase 3 study of patients with M0 CRPC and a PSADT ≤10 mo showed apalutamide (240 mg/day) improved the primary endpoint of metastasis-free survival over placebo (40.5 mo vs. 16.2 mo). No significant difference was seen in overall survival. Adverse events included rash (24% vs 5.5%), fracture (11% vs. 6.5%), and hypothyroidism (8% vs. 2%). Patients with M0 CRPC can be offered apalutamide after a discussion of the risks and benefits. Bone support should be used in patients receiving apalutamide.” (PROS-F, 3 of 4)

Previous updates to the NCCN Guidelines for Prostate Cancer can be found in the UPDATES section of the current version.

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Ovarian Cancer. These NCCN Guidelines® are currently available as Version 2.2018.

• The following single-agent recurrence therapy options for epithelial ovarian cancer (including LCOH/Fallopian tube/primary peritoneal cancer) have been moved from the "useful in certain circumstances" list (OV-B, 7 of 10) to the "other potentially active agents" list (OV-B, 6 of 10), and the recommended use criteria for each agent have been removed:
  - Carboplatin (for platinum-sensitive disease)
  - Cisplatin (for platinum-sensitive disease)
  - Paclitaxel, albumin-bound

Previous updates to the NCCN Guidelines for Ovarian Cancer can be found in the UPDATES section of the current version.
NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Acute Lymphoblastic Leukemia. These NCCN Guidelines® are currently available as Version 1.2018.

- **Diagnosis (ALL-1)**
  - Footnote e added: If there are sufficient numbers of circulating lymphoblasts (at least 1,000 per microliter as a general guideline) and clinical situation precludes bone marrow aspirate and biopsy, then peripheral blood can be substituted for bone marrow.
  - Footnote g modified: The Ph-like phenotype is associated with recurrent gene fusions and mutations that activate tyrosine kinase pathways and includes gene fusions involving ABL1, ABL2, CRLF2, CSF1R, EPOR, JAK2, or PDGFRB and mutations involving FLT3, IL7R, SH2B3, JAK1, JAK3, and JAK2 (in combination with CRLF2 gene fusions). Testing for these abnormalities at diagnosis may aid in risk stratification. The safety and efficacy of targeted agents in this population is an area of active research. For more information regarding Ph-like ALL, please see the Discussion.

- **Ph-positive ALL (Adult) (ALL-4)**
  - Treatment induction
    - TKI + corticosteroids added as a treatment option.

- **Ph-negative ALL (AYA) (ALL-5 and ALL-7)**
  - Consolidation therapy
    - Footnote aa added: The prognostic significance of MRD positivity may be regimen, ALL subtype, and/or ALL risk dependent. MRD time points and levels prompting allogeneic HCT should be guided by the specific treatment protocol being used. In general, MRD positivity at the end of induction predicts high relapse rates and should prompt evaluation for allogeneic HCT. Therapy aimed at eliminating MRD prior to allogeneic HCT is preferred when possible.

- **Relapsed/Refractory ALL (ALL-9)**
  - Treatment
    - Consider HCT added after all treatment options for Ph-positive and Ph-negative ALL
    - Footnote ii added: If second remission is achieved prior to transplant and patient has not had a prior HCT, consolidative HCT should be strongly considered.
    - Footnote kk added: The role of allogeneic HCT following tisagenlecleucel is unclear. Persistence of tisagenlecleucel in peripheral blood and persistent B-cell aplasia has been associated with durable clinical responses without subsequent HCT. In the global registration trial, relapse free survival was 59% at 12 months, with only 9% of patients proceeding to HCT.
    - Ph-positive ALL (AYA and Adult)
      - Blinatumomab indication modified
    - After failure of 2 TKIs changed to TKI intolerant/refractory

- **Induction Regimens for Ph-positive ALL (ALL-D 1 of 6)**
  - Protocols for AYA patients
    - The following regimen removed: COG AALL-0031 regimen: vincristine, prednisone (or dexamethasone), and pegaspargase, with or without daunorubicin; or prednisone or dexamethasone) and pegaspargase with or without daunorubicin; imatinib added during consolidation blocks
  - Maintenance regimens
    - Bullet 1 modified: Add TKIs (imatinib, dasatinib, nilotinib, ponatinib) to maintenance regimen for a minimum of 1 year, optimal duration is unknown.

- **Regimens for Relapsed or Refractory ALL (ALL-D 4 of 6)**
  - Fludarabine-based regimens with references added for Ph-negative ALL
- FLAG-IDA: fludarabine, cytarabine, granulocyte colony-stimulating factor, ± idarubicin
- FLAM: fludarabine, cytarabine, and mitoxantrone

Treatment of Older Adults with ALL (ALL-D 6 of 6)
- Induction regimens with references added for Ph-positive ALL in adults aged ≥65 years
  - Nilotinib ± steroids
  - GRALL regimen: doxorubicin, vincristine, dexamethasone, cytarabine, cyclophosphamide

March 8, 2018
NCCN has published updates to the following NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) with NCCN Evidence Blocks™:

- Testicular Cancer, Version 2.2018

Previous updates to the NCCN Guidelines for Testicular Cancer can be found in the UPDATES section of the current version.

March 2, 2018
NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Myeloid Growth Factors. These NCCN Guidelines® are currently available as Version 1.2018.

- CMF classic (cyclophosphamide, methotrexate, fluorouracil) has been removed from the list of examples of breast cancer regimens with an intermediate risk of febrile neutropenia. (MGF-A, 2 of 4)
- The following recommendation has been revised regarding the dose delivery of prophylactic pegfilgrastim: "For patients who cannot return to the clinic for next-day administration, alternative options exist that are FDA-approved delivery devices available that can be applied the same day as chemotherapy in order to deliver the full dose of pegfilgrastim the following day (approximately 27 hours after application)." (MGF-B)
- The following statement has been added regarding the use of myeloid growth factors in mobilization: "Effective mobilization regimens include growth factor alone, chemotherapy and growth factor combined, and incorporation of plerixafor with either approach." (MGF-D, 1 of 4)
- Myeloid Growth Factors in Mobilization and Post Hematopoietic Cell Transplant
  - Recommendations for use, dosing, and timing of administration of plerixafor have been updated. (MGF-D, 1 of 4)
  - The settings for which filgrastim or filgrastim-sndz or tbo-filgrastim are recommended as supportive care options has been expanded to include post haploidentical transplant. (MGF-D, 2 of 4)
  - Sargramostim has been removed from the post-transplant supportive care options. (MGF-D, 2 of 4)
- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)
February 28, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Ovarian Cancer. These NCCN Guidelines® are currently available as Version 1.2018.

- CA 19-9 has been added to the list of other tumor markers to be tested as clinically indicated during the workup for ovarian cancer. (OV-1 and OV-2)
- Footnote “n” has been revised: Pathologists recommend categorizing serous ovarian cancer as either low grade (most grade 1 serous tumors) or high grade (most grade 2 or 3 serous tumors). Grade 2 serous is considered high grade.” (OV-2 and OV-3).

Primary Chemotherapy/Primary adjuvant therapy (OV-3)

- The primary therapy options for stage IA-IB, grade 2 endometrioid tumors have been revised: “Observe or Intravenous (IV) platinum-based therapy taxane/carboplatin x 3–6 cycles (see primary regimens for stage I disease (OV-B, 3 of 10).”
- The primary therapy recommendation for stage IA-IB, grade 3 and stage IC, grade 1-3 tumors has been revised: “IV platinum-based therapy taxane/carboplatin x 3–6 cycles (see primary regimens for stage I disease (OV-B, 3 of 10).”
- The following primary therapy option for stage II-IV disease has been revised: “Platinum-based chemotherapy [See Primary Regimens for stage II-IV disease (OV-B, 3 of 10)] intraperitoneal (IP) chemotherapy in <1 cm optimally debulked stage II and stage III patients (category 1 for stage III, category 2A for stage II and LCOH) or IV taxane/carboplatin for a total of 6 cycles (category 1, category 2A for LCOH).”

Stage II-IV, Post Primary Treatment (OV-4)

- Bevacizumab has been added as a maintenance therapy option if partial or complete remission following systemic therapy with bevacizumab.
- Pazopanib has been changed from a category 2B to a category 3 maintenance therapy option if complete clinical remission following primary therapy for patients that did not previously receive bevacizumab.
- Paclitaxel has been removed from the maintenance therapy options if complete clinical remission following primary therapy for patients that did not previously receive bevacizumab.

Therapy for Persistent Disease or Recurrence (OV-6)

- Following complete remission and relapse ≥6 months after completing prior chemotherapy:
  - Continuation of bevacizumab has been added as a maintenance therapy option for patients with a partial or complete response following platinum-based recurrence chemotherapy with bevacizumab.
  - Rucaparib has been added as a maintenance therapy option for consideration for patients with a partial or complete response following 2 or more lines of platinum-based therapy.
- A category has been added under disease status to clarify the options for patients with progression following recurrence therapy for platinum-sensitive disease. The options include clinical trial and/or best supportive care and/or recurrence therapy.
Footnote “aa” has been added: “During and after treatment for recurrence, patients should be evaluated regularly with tumor markers and repeat imaging (with modalities previously used) to document response and/or disease status.”

The following has been added to footnote “ff”: “Discontinue bevacizumab before initiating maintenance therapy with a PARP inhibitor.”

- Clear Cell Carcinoma of the Ovary (LCOH-3)
  - The primary therapy recommendation for stage IA-IC tumors has been revised: “IV platinum-based therapy taxane/carboplatin x 3–6 cycles (see primary regimens for stage I disease (OV-B, 3 of 10).” (Also for stage IC on LCOH-4 and LCOH-5)

- Mucinous Carcinoma (LCOH-4)
  - 5-FU + leucovorin + oxaliplatin + bevacizumab has been added as a category 2B adjuvant therapy option for stage II-IV disease.
  - Capecitabine + oxaliplatin + bevacizumab has been added as a category 2B adjuvant therapy option for stage II-IV disease.

- Low-grade Serous/Grade 1 Endometrioid Epithelial Carcinoma (LCOH-5)
  - Exemestane has been added as an aromatase inhibitor option for stage IC-IV disease. This is a category 2B recommendation.
  - Maintenance hormonal therapy (ie, aromatase inhibitors [anastrozole, letrozole, exemestane], leuprolide acetate, tamoxifen) has been added as an option following chemotherapy for stage II-IV disease. This is a category 2B recommendation.


- Primary Systemic Therapy
  - The following IV regimens have been added as options for elderly patients (>age 70) and/or those with comorbidities, if stage I-IV epithelial ovarian cancer (including LCOH)/Fallopian Tube/Primary Peritoneal Cancer (OB-V, 2 of 10):
    - Carboplatin AUC 5 given every 3 wk
    - Paclitaxel 135 mg/m² + carboplatin AUC 5 given every 3 wk
    - Paclitaxel 60 mg/m² IV over 1 hour followed by carboplatin AUC 2 IV over 30 minutes. Weekly for 18 wk
  - The following primary systemic therapy options have been added for stage I epithelial ovarian cancer (including LCOH)/Fallopian Tube/Primary Peritoneal Cancer (OV-B, 3 of 10):
    - Paclitaxel 175 mg/m² IV over 3 hours followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 3–6 cycles. (preferred)
    - Carboplatin AUC 5 + pegylated liposomal doxorubicin 30 mg/m² every 4 weeks for 3–6 cycles
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- Docetaxel 60–75 mg/m² IV over 1 hour followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles

  - The following regimens have been changed from category 1 to category 2A recommendations for stages II-IV epithelial ovarian cancer (including LCOH)/Fallopian Tube/Primary Peritoneal Cancer:
    - IP/IV Paclitaxel/cisplatin
    - IV Paclitaxel/carboplatin (weekly)
    - IV Dose-dense paclitaxel/carboplatin
    - IV Paclitaxel/carboplatin (every 3 weeks)
    - IV Docetaxel/carboplatin

  - The bevacizumab-containing regimens (paclitaxel/carboplatin/bevacizumab) per ICON-7 and GOG-218 have been changed from category 2B to category 2A recommendations.

  - Under neoadjuvant therapy:
    - The following has been added: “Consider the histology of the primary tumor and the potential response to primary chemotherapy when evaluating for neoadjuvant chemotherapy.” (OV-B, 3 of 10)
    - The following has been added to the third bullet: “If bevacizumab is being used as part of a neoadjuvant regimen, bevacizumab should be withheld from therapy for at least 6 weeks prior to interval debulking surgery (IDS).” (OV-B, 3 of 10)

- Acceptable Recurrence Therapies for Epithelial Ovarian Cancer (including LCOH)/Fallopian Tube/Primary Peritoneal Cancer

  - Carboplatin/paclitaxel/bevacizumab has been moved from the other potentially active recurrence therapies to the list of preferred recurrence therapy options for platinum-sensitive disease. (OV-B, 5 of 10)

  - Carboplatin/paclitaxel has been changed from a category 1 to a category 2A preferred recurrence therapy option. (OV-B, 5 of 10)

  - Carboplatin/liposomal doxorubicin has been changed from a category 1 to a category 2A preferred recurrence therapy option. (OV-B, 5 of 10)

  - A new table has been added for options that are useful in certain circumstances. Some regimens included in this new table were previously included in the lists of “preferred agents” and “other potentially active agents.” (OV-B, 7 of 10)

- Exemestane has been added to the aromatase inhibitor recurrence therapy options for malignant sex cord-stromal tumors. (OV-B, 8 of 10)

- A table has been added with the maintenance therapy options considered useful in certain circumstances for epithelial ovarian cancer (including LCOH)/Fallopian tube/primary peritoneal cancer. (OV-B, 9 of 10)

NCCN has updated the NCCN Radiation Therapy Compendium™ to reflect recommendations within the following NCCN Guidelines:

- Anal Carcinoma version 1.2018
February 27, 2018

NCCN has published updates to the NCCN Guidelines and the NCCN Radiation Therapy Compendium™ for Malignant Pleural Mesothelioma. These NCCN Guidelines are currently available as Version 2.2018.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

Previous updates to the NCCN Guidelines for Malignant Pleural Mesothelioma can be found in the UPDATES section of the current version.

February 26, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas. These NCCN Guidelines® are currently available as Version 2.2018.

- Mantle cell lymphoma
  - Induction therapy heading was revised, "Suggested Treatment Regimens (in preference order)." (MANT-A 1 of 4)
  - Second-line therapy heading was revised, "Suggested Treatment Regimens (in preference order)" and "in alphabetical order" and "in alphabetical order by category" was added to the regimen list as appropriate. (MANT-A 2 of 4)

Previous updates to the NCCN Guidelines for B-Cell Lymphomas can be found in the UPDATES section of the current version.

February 23, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Radiation Therapy Compendium™ for T-Cell Lymphomas. These NCCN Guidelines® are currently available as Version 3.2018.

- Mycosis Fungoides/Sezary Syndrome
  - Skin-directed therapies (MFSS-A)
    - Local radiation was clarified from "8–36 Gy" to "(8-12 Gy; 24-30 Gy for unilesional presentation)." Also for MFSS-C.
  - The discussion section was updated for the following subtypes to reflect the changes in the algorithm. (MS-1)
    - Mycosis Fungoides/Sezary Syndrome (MFSS)
Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders (PCTLD)
- Adult T-Cell Leukemia/Lymphoma (ATLL)
- T-Cell Prolymphocytic Leukemia (TPLL)

Previous updates to the NCCN Guidelines for T-Cell Lymphomas can be found in the UPDATES section of the current version.

NCCN has published updates to the NCCN Guidelines for Cancer-Related Fatigue. These NCCN Guidelines are currently available as Version 2.2018.
- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

Previous updates to the NCCN Guidelines for Cancer-Related Fatigue can be found in the UPDATES section of the current version.

February 22, 2018
NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Distress Management. These NCCN Guidelines® are currently available as Version 2.2018.
- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

Previous updates to the NCCN Guidelines for Distress Management can be found in the UPDATES section of the current version.

February 20, 2018
NCCN has updated the NCCN Radiation Therapy Compendium™ to reflect recommendations within the following NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®):
- Cervical Cancer version 1.2018
- Uterine Neoplasms version 1.2018
- Vulvar Cancer version 1.2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Testicular Cancer. These NCCN Guidelines® are currently available as Version 2.2018.
- The Discussion has been updated to reflect the changes in the algorithm.

*Previous updates to the NCCN Guidelines for Testicular Cancer can be found in the UPDATES section of the current version.
NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Survivorship. These NCCN Guidelines® are currently available as Version 3.2017.

- **General Survivorship Principles**
  - Survivorship Assessment (Patient Version) (SURV-A)
    - “Lymphedema” was added to the list of “Survivorship Concerns” and the following corresponding questions were included:
      - Did your cancer treatment include radiation or surgery to the lymph nodes in your armpit, groin, abdomen, or neck (including sentinel lymph node biopsy)? Yes/No/Don’t know
      - Since your cancer treatment, have you had any swelling, fatigue, heaviness, or fullness on the same side as your treatment that has not gone away? Yes/No

- **Late Effects/Long-Term Psychosocial and Physical Problems**
  - Lymphedema
    - A new algorithm that provides recommendations for symptom assessment, workup, treatment, and surveillance of lymphedema in survivors was added. (SLYMPH-1)

  - A new section was added to the Discussion text to correspond to the new lymphedema algorithm. (MS-1)

* Previous updates to the NCCN Guidelines for Survivorship can be found in the UPDATES section of the current version.

February 16, 2018

NCCN has published NCCN Chemotherapy Order Templates (NCCN Templates®) for Acute Lymphoblastic Leukemia to reflect the currently published NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia, Version 5.2017.

- The following NEW NCCN Templates® have been published:
  - ALL26 – Nelarabine
  - ALL35a – Blinatumomab Induction
  - ALL35b – Blinatumomab Consolidation
  - ALL35c – Blinatumomab Continued Therapy
  - ALL38 – VinCRIStine Sulfate LIPOSOME Injection

NCCN has updated the NCCN Radiation Therapy Compendium™ to reflect recommendations within the
following NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®):

- Melanoma, Version 2.2018

NCCN has published updates to the NCCN Guidelines® and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Hepatobiliary Cancers. These NCCN Guidelines are currently available as Version 1.2018.

- Hepatocellular Carcinoma
  - Screening for patients at risk for HCC (HCC-1)
  - Treatment for patients ineligible for transplant (HCC-4)
    - A bullet was amended: "External-beam radiation therapy (EBRT) (category 2B) Radiation therapy, and accompanying footnote was also amended: "Case series and single-arm studies demonstrate safety and possible efficacy of radiation therapy in selected cases. See Principles of Locoregional Therapy (HCC-E)." (Also for HCC-5 and HCC-6)
  - Principles of Imaging, Extrahepatic Staging (HCC-A)
    - A statement was amended: "Frequent sites of extrahepatic metastases from HCC include lungs, and bone and lymph nodes. Adrenal and peritoneal metastases also may occur. For this reason, chest CT, complete imaging of abdomen and pelvis with contrast-enhanced CT or MRI, and selective use of bone scan when skeletal symptoms are present are recommended at initial diagnosis of HCC and for monitoring disease while on the transplant wait list or during or after treatment for response assessment. Chest CT may be performed with contrast if concurrently acquired with contrast-enhanced abdominal/pelvic CT. If MRI is performed, chest CT may be acquired without contrast."
  - Principles of Locoregional Therapy
    - A sub-bullet was amended: "Arterially directed therapies are relatively contraindicated in highly selected patients have been shown to be safe in the presence of limited tumor invasion with main of the portal vein, thrombosis and Child-Pugh Class C." (HCC-E 1 of 3)
    - The title "External-beam Radiation Therapy (EBRT)" was revised. (HCC-E 2 of 3)
      - A bullet was added: "Dosing for SBRT is generally is 30-50 Gy in 3-5 fractions, depending on the ability to meet normal organ constraints and underlying liver function. Other hypofractionated schedules >5 fractions may also be used if clinically indicated."

- Gallbladder Cancer
  - A bullet was added for unresectable disease, jaundice, and metastatic disease: "Microsatellite instability (MSI) testing" (GALL-1, GALL-2, GALL-3, and GALL-4)
  - Primary treatment, unresectable and metastatic disease
    - A bullet was amended: "EBRT Radiation therapy"(GALL-1, GALL-2, GALL-3, GALL-4, and INTRA-1)
      - A bullet: "Pembrolizumab (Only for MSI-H tumors)" was added a treatment option, with an accompanying footnote: "There are limited clinical trial data to support pembrolizumab in this setting. Personalized, molecularly matched combination therapies for treatment-naive, lethal malignancies:

- Treatment (GALL-5)
  - Resected, positive margin (R1) or Resected gross residual disease (R2) or Positive regional nodes
    - A statement was amended: "Consider Fluoropyrimidine chemoradiation followed by additional fluoropyrimidine-based or gemcitabine-based chemotherapy or Fluoropyrimidine-based or gemcitabine-based chemotherapy+/- fluoropyrimidine chemoradiation for positive regional lymph nodes or Clinical trial" and supporting reference was added: "Ben-Josef E, Guthrie KA, El-Khoueiry AB, et al. SWOG S0809: A phase II intergroup trial of adjuvant capcitabine and gemcitabine followed by radiotherapy and concurrent capcitabine in extrahepatic cholangiocarcinoma and gallbladder carcinoma. J Clin Oncol 2015;33(24):2617-2622." (Also for INTRA-2 and EXTRA-2)
  - For chemotherapy in the adjuvant setting, the footnote was amended: "There are no randomized phase III clinical trial data to support a standard adjuvant regimen. Clinical trial participation is encouraged. There are phase II trials that support the following combinations: gemcitabine/cisplatin, gemcitabine/oxaliplatin, gemcitabine/capcitabine, capcitabine/cisplatin, capcitabine/oxaliplatin, 5-fluorouracil/oxaliplatin, 5-fluorouracil/cisplatin, and the single agents gemcitabine, capcitabine, and 5-fluorouracil in the unresectable or metastatic setting. (Hezel AF and Zhu AX. Systemic therapy for biliary tract cancers. Oncologist 2008;13:415-423). The phase 3 BILCAP study shows improved overall survival for adjuvant capcitabine in the per-protocol analysis, but the study is not yet published, and the overall survival did not reach statistical significance in the intent-to-treat analysis. Primrose JN, Fox R, Palmer DH, et al: Adjuvant Capecitabine for Biliary Tract Cancer. The BILCAP randomized study. ASCO Meeting 2017. Abstract 4006." (Also for INTRA-2 and EXTRA-2)

- Principles of Radiation Therapy (GALL-C)
  - A bullet under “Adjuvant EBRT” was revised: “Target volumes should cover the draining regional lymph nodes to 45 Gy at 1.8 Gy/fraction and 50.4–59.4 at 1.8 Gy/fraction 50–60 Gy in 1.8–2 Gy/fraction to the tumor bed depending on margin positivity.”
  - A bullet under “Unresectable” was amended: “Dosing for SBRT for biliary tract tumors is generally 30-50 Gy in 3-5 fractions, depending on the ability to meet normal organ constraints and underlying liver function. Other hypofractionated schedules >5 fractions may also be used if clinically indicated. For intrahepatic tumors, SBRT in 1-5 fractions is an acceptable option.”

- Intrahepatic Cholangiocarcinoma
  - A bullet was added for Unresectable and Metastatic disease: “Consider molecular testing, including MSI testing.” (INTRA-1, also for EXTRA-1)
  - Primary Treatment, Unresectable and Metastatic disease (INTRA-1)
    - Treatment options statement was revised: “Consider locoregional therapy (category 2B)”
    - “Arterially directed therapies” was added as a treatment option for metastatic disease

- Extrahepatic Cholangiocarcinoma
  - A primary treatment option was added for unresectable disease: “Radiation therapy” (EXTRA-1)

- Staging Tables (ST-1)
  - Staging tables have been revised to reflect the 8th edition of the AJCC Cancer Staging System.
NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Head and Neck Cancers. These NCCN Guidelines® are currently available as Version 1.2018.

- **Cancer of the Lip**
  - Sentinel lymph node biopsy (category 2B) has been removed from the primary therapy options for T1-2, N0 disease. (LIP-2)
  - RT has been added as an adjuvant therapy option for patients with perineural/vascular/lymphatic invasion following surgical resection of a T1-2, N0 lesion. (LIP-2)

- **Cancer of the Oral Cavity**
  - For patients with T3, N0; T1-3, N1-3; T4a, any N disease, RT has been removed as an adjuvant treatment option for those with extranodal extension with or without a positive margin. (OR-3)

- **Cancer of the Oropharynx**
  - Workup and Clinical Staging (ORPH-1)
    - The first bullet has been revised: "Tumor human papillomavirus (HPV) testing by p16 immunohistochemistry (IHC) required."
    - New pathways have been included for p16-negative and p16 (HPV)-positive disease.
    - Footnote "g" has been added: "The clinical staging definitions take into consideration the new AJCC 8th edition staging for oropharynx cancer, while referencing the staging criteria previously used in clinical trials on the management of oropharynx cancer."
  - For p16-negative oropharyngeal cancer, the inclusion criteria have been revised for the option of RT + systemic therapy. The treatment option now reads, "For T1-T2, N1 only: RT + systemic therapy (category 2B for systemic therapy)." (OR-PH-2)
  - New pages have been added with recommendations for p16 (HPV)-positive cancers of the oropharynx. (ORPHPV-1)
  - A new section has been added, titled, "Principles of p16 testing for HPV-mediated oropharyngeal cancer." (ORPH-B)

- **Cancer of the Hypopharynx**
  - Surgery recommendations have been revised and lymph node dissection recommendations have been clarified. (HYPO-1, HYPO-3, HYPO-5, GLOT-3, GLOT-6)

- **Cancer of the Nasopharynx**
  - For T1, N1-3 disease, or T2-4, any N disease, the option of induction chemotherapy followed by chemo/RT has been changed from a category 3 recommendation to a category 2A. (NASO-2) (Also CHEM-A, 1 of 5)
  - The following has been added to the Principles of Radiation Therapy: "Proton therapy can be considered when normal tissue constraints cannot be met by photon-based therapy." (NASO-A) (Also on ETHM-A, MAXI-A, ADV-A, SALI-A, and MM-A)

- **Cancer of the Glottic Larynx**
Following surgery for stage T4a, any N disease, adjuvant therapy options have been added for those with adverse features (GLOT-6).

- **Ethmoid Sinus Tumors**
  - An adjuvant therapy option has been added for those diagnosed after incomplete resection with no residual disease on physical exam, imaging and/or endoscopy, following primary surgery: "Consider systemic therapy/RT (category 2B) if adverse features." (ETHM-3)

- **Maxillary Sinus Tumors**
  - The following footnote has been removed for patients with T3-T4a, N0 disease: "For surgical resection, consider preoperative RT or preoperative systemic therapy/RT in select patients (category 2B)." (MAXI-3)

- **Very Advanced Head and Neck Cancer**
  - The following primary treatment option has been added for those with a resectable locoregional recurrence without prior RT: "Induction chemotherapy (category 3) followed by RT or systemic therapy/RT." (ADV-3)
  - Footnote "c" has been added: "When using concurrent systemic therapy/RT, the preferred agent is cisplatin (category 1). See Principles of Systemic Therapy (CHEM-A)." (ADV-3)

- **Occult Primary**
  - For a level IV or V adenocarcinoma of neck node, after evaluation for infraclavicular primary, the definitive treatment has been revised: "Neck dissection if indicated + adjuvant treatment if indicated (see OCC-4)." (OCC-2)
  - Indications have been revised for the following treatment options for poorly differentiated or nonkeratinizing squamous cell or not otherwise specified, or anaplastic (not thyroid), or squamous cell carcinoma:
    - "Neck dissection (preferred for N1 disease, single node ≤3 cm)"
    - "RT for N1, single node ≤3 cm (category 2B)"
    - "Induction chemotherapy for N2-3 (category 3) followed by systemic therapy/RT or RT"

- **Salivary Gland Tumors**
  - Footnote "m" has been added for those with distant metastases: "Check androgen receptor (AR) status and HER2 status prior to treatment for distant metastases." (SALI-4)
  - The following recurrence therapy options have been added for those with distant metastases and PS 0-3:
    - Androgen receptor (AR) therapy (ie. leuprolide, bicalutamide) if AR+
    - Trastuzumab if HER2+ (category 2B)

- **Radiation Techniques**
  - Standard reirradiation doses have been added for 3D conformal RT and IMRT: “59.4–60 Gy at 1.8–2 Gy/fraction. Hyperfractionated schedule is 60 Gy at 1.2–1.5 Gy/fraction.” (RAD-A, 3 of 5)

- **Principles of Systemic Therapy**
  - Weekly cisplatin (category 2B) has been added as an option to be used with concurrent chemoradiation following induction chemotherapy for cancers of the lip, oral cavity, oropharynx, hypopharynx, glottic larynx, supraglottic larynx, ethmoid sinus, maxillary sinus, and occult primary tumors. (CHEM-A, 1 of 5)
  - Systemic therapy for recurrent, unresectable or metastatic disease (with no surgery or RT option) (CHEM-A, 2 of 5):
Options have been reorganized to include first-line therapy options and second-line or subsequent therapy options.

- Cisplatin/gemcitabine has been changed from a category 2A to a category 1 option for nasopharyngeal cancer.
- Gemcitabine/vinorelbine has been removed from the therapy options for nasopharyngeal cancer.
- Pembrolizumab has been added as a category 2B subsequent therapy option for those with previously treated, PD-L1-positive recurrent or metastatic nasopharyngeal cancer.

**Principles of Nutrition**

- The following pain management recommendation has been added, including supporting references: “Assess pain from oral mucositis and prescribe gabapentin or doxepin as clinically indicated.” (NUTRA-A, 1 of 2)

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), NCCN Chemotherapy Order Templates (NCCN Templates®) and NCCN Drugs & Biologics Compendium (NCCN Compendium®) for B-Cell Lymphomas. These NCCN Guidelines® are currently available as Version 1.2018.

**General**

- The common bullets related to diagnosis were removed for each subtype and added to a new page, DIAG-1. For each subtype, the diagnosis section is now titled, “Additional Diagnostic Testing.”

**Follicular Lymphoma**

- Pediatric-Type Follicular Lymphoma in Adults (FOLL-8)
  - Treatment with CHOP was qualified by adding, "for patients with extensive local disease who are not candidates for excision or ISRT."
- First-line Therapy (FOLL-B 1 of 4)
  - The regimens were separated into "preferred regimens" and "other recommended regimens" and listed in alphabetical order.
  - Bendamustine + rituximab was changed from a category 1 to a category 2A recommendation.
  - RCHOP was changed from a category 1 to a category 2A recommendation.
  - RCVP was changed from a category 1 to a category 2A recommendation.
- First-line Consolidation or Extended Dosing (optional) (FOLL-B 1 of 4)
  - Ibritumomab tiuxetan was revised by removing, "(after induction with chemotherapy or chemoimmunotherapy)."
- Second-line and Subsequent Therapy (FOLL-B 2 of 4)
  - The regimens were separated into "preferred regimens" and "other recommended regimens."
  - Ibritumomab tiuxetan was changed from a category 1 to a category 2A recommendation.
  - The following regimens were removed:
    - Fludarabine + rituximab
    - RFND (rituximab, fludarabine, mitoxantrone, dexamethasone)

**Marginal Zone Lymphoma (MZL)**
• Splenic MZL (SPLN-2): For splenomegaly, hepatitis C negative, cytopenias and symptoms present, "preferred" was added to rituximab and "if not responsive to rituximab" was added to splenectomy.

• Suggested Treatment Regimens (First-line Therapy (MZL-A 1 of 3))
  ▪ The regimens were separated into "preferred regimens" and "other recommended regimens." These were placed in alphabetical order.
    ▪ "Preferred for SMZL" was added to "rituximab (375 mg/m² weekly for 4 doses)."
    ▪ The following were added as "other recommended regimens"
      o Lenalidomide + rituximab as a category 2B recommendation
      o Ibrutinomab tiuxetan as a category 2B recommendation.

• Mantle Cell Lymphoma (MCL)
  o First-line Therapy (MANT-A 1 of 4)
    ▪ Induction therapy
      ▪ For both aggressive and less aggressive therapy, the regimens were separated into "preferred regimens" and "other recommended regimens" and listed in preference order.
      ▪ Aggressive therapy
        o Footnote was removed, "Oxaliplatin or carboplatin can also be used" and oxaliplatin was added to the regimen RDHAX (rituximab, dexamethasone, cytarabine, oxaliplatin) as an alternative to RDHAP.
        o HyperCVAD, "(NOTE: There are conflicting data regarding the need for consolidation with HDT/ASCR.)" was added to the bullet.
        o Bendamustine + rituximab was added as a category 2B recommendation.
        o The following regimens were removed:
          ▪ CALGB regimen
          ▪ Sequential RCHOP/RICE
    ▪ Less aggressive therapy
      o RBAC (rituximab, bendamustine, cytarabine) was added as a category 2B recommendation.
      o Cladribine + rituximab was removed.
  o Second-line Therapy (MANT-A 2 of 4)
    ▪ The regimens were reorganized first by "Short response duration to prior chemoimmunotherapy (< expected median PFS)" and "Extended response duration to prior chemoimmunotherapy (> expected median PFS)." Then the regimens were separated into "preferred regimens" and "other recommended regimens."
    ▪ The following regimens were added or revised,
      ▪ RCHOP (if not previously given) (category 2B) was added.
      ▪ VRCAP (if not previously given) (category 2B) was added.
      ▪ "± rituximab" was added to ibrutinib.
      ▪ "(if not previously given)" was added to bendamustine ± rituximab.
    ▪ The following regimens were removed,
      ▪ Cladribine + rituximab
      ▪ FC (fludarabine, cyclophosphamide) ± rituximab
      ▪ PCR (pentostatin, cyclophosphamide, rituximab)
• Diffuse Large B-Cell Lymphoma (DLBCL)
  o Stage I, II, Non-bulky
    ▪ First-line therapy, “RCHOP-14 x 4–6 cycles” was added.
  o First-line Therapy (BCEL-C 1 of 4)
    ▪ Dose-adjusted EPOCH + rituximab was changed from a category 2B to category 2A recommendation.
    ▪ For very frail patients and patients >80 y of age with comorbidities, RCEPP and RCDOP were added as options.
  o Second-line and Subsequent Therapy (BCEL-C 2 of 4)
    ▪ For non-candidates for high-dose therapy, ibrutinib (non-GCB DLBCL) was added as an option with a category 2A recommendation.

• Burkitt Lymphoma
  o Relapsed/refractory disease (BURK-3): Recommendations for response assessment after second-line therapy and treatment options for consolidation/additional therapy were added.
  o Induction therapy, “CALGB 10002 regimen” was removed. (BURK-A)

• AIDS-Related B-cell Lymphomas
  o Burkitt lymphoma (AIDS-3)
    ▪ The regimens were separated into “preferred regimens” and “other recommended regimen.”
      ▪ “CDE (cyclophosphamide, doxorubicin, etoposide) + rituximab” was removed as an option.
      ▪ After treatment, a link was added regarding relapsed disease, “For relapse, see second-line regimens (BURK-A).”
  o Diffuse large B-cell lymphoma, HHV8-positive DLBCL, NOS and Primary effusion lymphoma (AIDS-3)
    ▪ “CDE + rituximab” was removed as an option.
  o Plasmablastic lymphoma (AIDS-4)
    ▪ “Preferred” was added to “dose-adjusted EPOCH.”
    ▪ The 3rd bullet was added, “Consider high-dose therapy with autologous stem cell rescue in first complete remission in select high-risk patients.”

• Castleman’s Disease
  o Multicentric (CD-3)
    ▪ Primary treatment, the 2nd bullet was added, “Rituximab (if not candidate for combination therapy).”

• Supportive Care for B-Cell Lymphomas
  o A new page titled, “Bone Health: Recommendations for Patients Who Have Received Steroid-Containing Regimens” was added. (NHODG-B 4 of 4)

• Principles of Radiation Therapy
  o The following general dose guidelines were added,
• Palliative RT (higher doses/fractions typically appropriate))
  • FL/MZL/MCL: 2 Gy X 2 or 4 Gy X 1 (which may be repeated as needed); doses up to 30 Gy may be appropriate in select circumstances
  • DLBCL: 24–30 Gy

The following NCCN Templates® have been deleted to reflect the NCCN Guidelines for B-Cell Lymphoma Version 1.2018:

• Follicular Lymphoma (grade 1-2)
  o FOL3: Fludarabine + RiTUXimab
  o FOL4: FND (Fludarabine/MitoXANTRONE/Dexamethasone) + RiTUXimab

• Mantle Cell Lymphoma
  o MCL13: FC (Fludarabine/Cyclophosphamide)
  o MCL14: FCR (Fludarabine/Cyclophosphamide + RiTUXimab)
  o MCL15: PCR (Pentostatin/Cyclophosphamide + RiTUXimab)
  o MCL21: Cladribine + RiTUXimab
  o MCL22a: CALGB59909 Regimen: RiTUXIMAB + Methotrexate with Augmented CHOP (Cyclophosphamide/DOXOrubicin/VinCRISTine/PredniSONE)
  o MCL22b: CALGB59909 Regimen: RiTUXimab Maintenance
  o MCL23a: Dose-Dense R-CHOP-14 (RiTUXimab + Cyclophosphamide/DOXOrubicin/VinCRISTine/PredniSONE) followed by RICE (RiTUXimab + Ifosfamide/CARBOplatin/Etoposide)–Dose-Dense R-CHOP-14 (RiTUXimab + Cyclophosphamide/DOXOrubicin/VinCRISTine/PredniSONE) Course
  o MCL23b: Dose-Dense R-CHOP-14 (RiTUXimab + Cyclophosphamide/DOXOrubicin/VinCRISTine/PredniSONE) followed by RICE (RiTUXimab + Ifosfamide/CARBOplatin/Etoposide)–RICE (RiTUXImab + Ifosfamide/CARBOplatin/Etoposide) Course

February 13, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Multiple Myeloma. These NCCN Guidelines® are currently available as Version 4.2018.

• Active (symptomatic) myeloma, primary treatment (MYEL-4)
  o Added denosumab as an option for the prevention of skeletal-related events for all patients receiving primary treatment.

• Supportive care treatment for multiple myeloma, bone disease (MYEL-E)
  o Removed the bullet “Bisphosphonates (pamidronate and zoledronic acid).”
  o Modified “All patients receiving primary myeloma therapy should be given bisphosphonates (category 1)” by adding “or denosumab.”
  o Modified “A baseline dental exam is recommended,” removed before starting bisphosphonate therapy.
  o Added a new footnote “Denosumab is preferred in patients with renal insufficiency.”
Previous updates to the NCCN Guidelines for Multiple Myeloma can be found in the UPDATES section of the current version.

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), NCCN Guidelines® with NCCN Evidence Blocks™, and NCCN Radiation Therapy Compendium™ for Breast Cancer. These NCCN Guidelines for Breast Cancer are currently available as Version 4.2017.

- **Ductal Carcinoma In Situ (DCIS)**
  - Primary treatment (DCIS-1)
    - Clarified the following recommendation by moving the placement of (category 1): Lumpectomy without lymph node surgery + whole breast radiation therapy (category 1) with or without boost to tumor bed.
    - Modified footnote e: “Re-resection(s) may be performed in an effort to obtain negative margins in patients desiring breast-conserving therapy. Patients in whom adequate surgical margins cannot be achieved with lumpectomy should undergo a total mastectomy. For definition of adequate surgical margins, see Margin Status Recommendations for DCIS and Invasive Breast Cancer (BINV-F)."
    - Modified footnote f: “Complete axillary lymph node dissection should not be performed in the absence of evidence of invasive cancer or proven axillary metastatic disease in women with apparent pure DCIS. However, a small proportion of patients with apparent pure DCIS will be found to have invasive cancer at the time of their definitive surgical procedure. Therefore, the performance of a sentinel lymph node procedure should be strongly considered if the patient with apparent pure DCIS is to be treated with mastectomy or with excision in an anatomic location compromising the performance of a future sentinel lymph node procedure.”

- **Invasive Breast Cancer Preoperative Systemic Therapy: Adjuvant Therapy**
  - Corrected recommendation for adjuvant therapy, post lumpectomy: “Strongly consider radiation to the whole breast + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk for clinical N1, ypN0.” (BINV-13)

- **Margin Status Recommendations for DCIS and Invasive Breast Cancer**
  - Modified bullet 2: “For mammographically-detected DCIS with microcalcifications, complete resection should be documented by analysis of margins and specimen radiography. Post-excision mammography could also be performed whenever uncertainty about adequacy of excision remains.” (BINV-F, page 1 of 2)

- **Discussion**
  - The DCIS content in the Discussion section has been updated to correspond with the DCIS algorithms. (MS-1)

Previous updates to the NCCN Guidelines for Bladder Cancer can be found in the UPDATES section of the current version.
February 12, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. These NCCN Guidelines® are currently available as Version 3.2018.

- Global changes to suggested treatment regimens
  - Regimens under each category of preference are listed in alphabetical order and by category of evidence and consensus

- CLL/SLL without del(17p)/TP53 mutation (CSLL-D 2 of 5)
  - Relapsed/refractory therapy
    - Preferred regimens
      - Venetoclax was changed from ± rituximab to venetoclax + rituximab and category of evidence and consensus was changed from a category 2A to a category 1 recommendation.
    - Other recommended regimens
      - Venetoclax as a single agent was moved from preferred to other and remains a category 2A recommendation.
      - Acalabrutinib was added as a category 2A recommendation with the following footnote: “Acalabrutinib should not be used for ibrutinib refractory CLL with BTK C481S mutations. Patients with ibrutinib intolerance have been successfully treated with acalabrutinib without recurrence of these symptoms.”
      - Footnote was removed from venetoclax with or without rituximab, “Particularly for patients deemed intolerant or refractory to ibrutinib or idelalisib.”

- CLL/SLL with del(17p)/TP53 mutation (CSLL-D 3 of 5)
  - Relapsed/refractory therapy
    - Preferred regimens
      - Ibrutinib was changed from a category 2A to a category 1 recommendation
      - Venetoclax was changed from ± rituximab to venetoclax + rituximab and category of evidence and consensus was changed from a category 2A to a category 1 recommendation
      - Venetoclax as single agent therapy remains a preferred regimen with a category 2A recommendation
    - Other recommended regimens
      - Acalabrutinib was added as a category 2A recommendation with the following footnote: “Acalabrutinib should not be used for ibrutinib refractory CLL with BTK C481S mutations. Patients with ibrutinib intolerance have been successfully treated with acalabrutinib without recurrence of these symptoms.”

- Special considerations for the use of small-molecule inhibitors (CSLL-F, 1 of 3)
  - Dosage and recommendations for management of toxicity related to acalabrutinib was added.
Previous updates to the NCCN Guidelines for CLL/SLL can be found in the UPDATES section of the current version.

February 8, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Kidney Cancer. These NCCN Guidelines® are currently available as Version 3.2018.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

Previous updates to the NCCN Guidelines for Kidney Cancer can be found in the UPDATES section of the current version.

NCCN has published updates to the NCCN Guidelines and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Bladder Cancer. These NCCN Guidelines are currently available as Version 2.2018.

- Upper GU Tract Tumors
  - Footnote f was clarified by adding a link to subsequent therapy options for locally advanced or metastatic disease (Stage IV) on BL-G 3 of 5. (UTT-1 and UTT-2)

- Urothelial Carcinoma of the Prostate
  - Footnote d was clarified by adding a link to subsequent therapy options for locally advanced or metastatic disease (Stage IV) on BL-G 3 of 5. (UCP-1)

Previous updates to the NCCN Guidelines for Bladder Cancer can be found in the UPDATES section of the current version.

NCCN has published updates to the NCCN Guidelines, NCCN Compendium®, and NCCN Imaging Appropriate Use Criteria (NCCN Imaging AUC™) for Malignant Pleural Mesothelioma. These NCCN Guidelines are currently available as Version 1.2018.

- Primary treatment (MPM-3)
  - Pemetrexed and carboplatin added as an induction chemotherapy option.

- Principles of Systemic Therapy (MPM-A)
  - First-line Combination Chemotherapy Regimens
    - Pemetrexed/carboplatin regimen modified with this addition
      - ± bevacizumab 15 mg/kg day 1
• ± maintenance bevacizumab 15 mg/kg (if bevacizumab given in combination with pemetrexed and carboplatin) every 3 weeks until disease progression.
• Footnote ** modified: The combination regimen of pemetrexed/cisplatin/bevacizumab or pemetrexed/carboplatin/bevacizumab is only for unresectable disease.
• Footnote removed: The carboplatin/pemetrexed regimen is recommended for patients with poor PS and/or comorbidities.
  o Subsequent Systemic Therapy
    ▪ Nivolumab ± ipilimumab: category changed from a category 2A to a category 2B.

• Principles of Surgery (MPM-C)
  o Bullet 8: the following has been added as the last sentence: P/D can provide excellent symptomatic control of recurrent pleural effusions.

• Staging updated to reflect the changes in the AJCC Cancer Staging Manual, Eighth Edition (2017). (ST-1)

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium™), the NCCN Radiation Therapy Compendium™, and the NCCN Imaging Appropriate Use Criteria (NCCN Imaging AUC™) for Anal Carcinoma. These NCCN Guidelines for Anal Carcinoma® are currently available as Version 1.2018.

• Metastatic Disease
  o Primary Treatment (ANAL-1, ANAL-2, ANAL-3, ANAL-4)
    ▪ The following regimens added as first-line treatment options
      • Carboplatin/paclitaxel ± RT (category 2A)
      • FOLFOX ± RT (category 2A)
    ▪ The following regimens added as subsequent therapy options
      • Nivolumab (category 2A)
      • Pembrolizumab (category 2A)

  o Inguinal Node Recurrence (ANAL-3)
    ▪ The following regimen added as a treatment option
      • 5-FU/cisplatin (category 2B)

  o New section added for Principles of Surgery (ANAL-A)

• Principles of Chemotherapy (ANAL-B)
  o Localized cancer
    ▪ The following regimen updated: 5-FU + cisplatin.
    ▪ Dosing for cisplatin changed from 100 mg/m² to 75 mg/m² on day 1 (from day 2) and dosing for 5-FU changed from days 1-5 to days 1-4. Reference updated.
  o Metastatic cancer
    ▪ Dosing for 5-FU + cisplatin changed. References updated.
    ▪ Previous regimen dosing:
      Cisplatin 100 mg/m² day 1
Continuous infusion 5-FU 1000 mg/m²/d IV days 1–5
Repeat every 4 weeks
• Updated regimen dosing:
  Cisplatin 60 mg/m² day 1
  Continuous infusion 5-FU 1000 mg/m²/d IV days 1–4
  Repeat every 3 weeks
  or
  Cisplatin 75 mg/m² day 1
  Continuous infusion 5-FU 750 mg/m²/d IV days 1–5
  Repeat every 4 weeks
• The following regimens added with references
  • mFOLFOX6
  • Carboplatin + paclitaxel
  • Nivolumab
  • Pembrolizumab

• Principles of Radiation Therapy (ANAL-C page 2 of 2)
  o Bullet 2 modified with this addition: Radiation therapy technique and doses are dependent on dosing and
technique of prior treatment. In the setting of pure palliation, doses of 20-25 Gy in 5 fractions to 30 Gy in
10 fractions can be considered. SBRT can also be considered for treatment of primary and nodal
recurrence in the setting of low volume metastatic disease.
  o Bullet 3 added: Image guidance (IGRT) with kilovoltage (kV) imaging and cone beam CT imaging should
be routinely used during the course of treatment with IMRT and SBRT.

• New section added for Principles of Survivorship (ANAL-D)

• Staging in the NCCN Guidelines for Anal Carcinoma (ST-1)

NCCN has published updates to the NCCN Guidelines and the NCCN Compendium® for Breast Cancer
Risk-Reduction. These NCCN Guidelines® are currently available as Version 1.2018.

• For Risk-reduction therapy follow-up, the last bullet was modified as follows: “Monitor bone density while on
aromatase inhibitors.” (BRISK-5)

• Osteopenia/osteoporosis are new “clinical scenarios” with the corresponding footnote, “Weight-bearing
exercise or use of a bisphosphonate (oral/IV) or denosumab is acceptable to maintain or to improve bone
mineral density and reduce risk of fractures in women receiving aromatase inhibitors. Women treated with a
bisphosphonate or denosumab should undergo a dental examination with preventive dentistry prior to the
initiation of therapy, and should take supplemental calcium and vitamin D.” (BRISK-7)

• Under Aromatase inhibitors (Exemestane and Anastrozole) the following bullet has been modified: “There is
retrospective data that AI’s can reduce the risk of contralateral breast cancer in BRCA-1/2 patients with ER
positive breast cancer who take AI’s as adjuvant therapy” (BRISK-B)
NCCN has published updates to the NCCN Chemotherapy Order Templates (NCCN Templates®) for Colon Cancer to reflect the currently published NCCN Guidelines for Colon Cancer Version 1.2018

- Indications for templates COL2 through COL49 have been revised to be more specific.

- Cycle information for the following templates have been revised as follows:
  - COL3: Roswell Park Fluorouracil/Leucovorin: 8-week cycle (6 weeks on followed by 2 weeks off treatment) for 4 cycles (adjuvant perioperative therapy) or until disease progression or unacceptable toxicity (advanced or metastatic).
  - COL4: Capecitabine: 21-day cycle for 8 cycles (adjuvant perioperative therapy) or until disease progression or unacceptable toxicity (advanced or metastatic).
  - COL10: Simplified Biweekly Infusional Fluorouracil/Leucovorin: 14-day cycle for 12 cycles (adjuvant perioperative therapy) or until disease progression or unacceptable toxicity (advanced or metastatic).
  - COL28: FOLFIRI (Fluorouracil Continuous Infusion/Leucovorin/Irinotecan): 14-day cycle for 8–12 cycles perioperative therapy or until disease progression or unacceptable toxicity.

- Recommendations based on age, performance status, and prior pelvic irradiation have been added to the irinotecan doses on the following templates:
  - COL18: Irinotecan Every 21 Days + Cetuximab
  - COL32: Irinotecan Every 21 Days

- The dose of continuous infusion fluorouracil has been reduced in the Chemotherapy Regimen section of the following template and a new note referencing that change has been added:
  - COL46: FOLFOXIRI (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin/Irinotecan)
    - European clinical trials used higher doses of fluorouracil in this regimen (3200 mg/m² over 48 hours). Patients in the United States (U.S.) have been shown to have a poorer tolerance for fluorouracil. The dose of fluorouracil on this template (2400 mg/m² over 48 hours) is a starting dose consistent with the dose recommended in FOLFOX or FOLFIRI and should be strongly considered for U.S. patients.

- Alternative infusion rate instructions for OXALIplatin have been added to the Safety Parameters and Special Instructions section of the following templates:
  - COL2: mFOLFOX6 (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin)
  - COL11: CapeOX (Capecitabine/OXALIplatin) + Bevacizumab
  - COL16: mFOLFOX6 (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin) + Bevacizumab
  - COL17: CapeOX (Capecitabine/OXALIplatin)
  - COL44: mFOLFOX6 (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin) + Cetuximab
  - COL46: FOLFOXIRI (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin/Irinotecan)
  - COL47: IROX (Irinotecan/OXALIplatin)
  - COL48: mFOLFOX6 (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin) + Panitumumab

- The following NEW note for leucovorin has been added to the Chemotherapy Regimen section of the following templates: “Leucovorin infusion time should match the infusion time of OXALIplatin when these agents are given concurrently.” This affects the following templates:
  - COL2: mFOLFOX6 (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin)
  - COL16: mFOLFOX6 (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin) + Bevacizumab
  - COL44: mFOLFOX6 (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin) + Cetuximab
  - COL46: FOLFOXIRI (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin/Irinotecan)
The following note for irinotecan has been updated in the Safety Parameters and Special Instructions section: “Patients who are homozygous for the UGT1A1*28 allele or who have a clinical diagnosis of Gilbert’s Syndrome have an increased risk of neutropenia when started on irinotecan, possibly due to a decreased level of glucuronidation of the active metabolite of irinotecan, resulting in its accumulation. Review drug package insert for clinical pharmacology, precautions, warnings, and recommendations.” This affects the following templates:

- COL14: FOLFIRI (Fluorouracil Continuous Infusion/Leucovorin/Irinotecan) + Bevacizumab
- COL18: Irinotecan Every 21 Days + Cetuximab
- COL19: Irinotecan Every 14 Days + Cetuximab
- COL20: Irinotecan Days 1 and 8 every 21 Days + Cetuximab
- COL22: FOLFIRI (Fluorouracil Continuous Infusion/Leucovorin/Irinotecan) + Cetuximab
- COL32: Irinotecan Every 21 Days
- COL33: Irinotecan Days 1 and 8 Every 21 Days
- COL46: FOLFOXIRI (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin/Irinotecan) + Bevacizumab
- COL47: IROX (Irinotecan/OXALIplatin)
- COL49: FOLFIRI (Fluorouracil Continuous Infusion/Leucovorin/Irinotecan) + Panitumumab

The following NEW note for irinotecan has been added to the Safety Parameters and Special Instructions section: “This agent has multiple potential drug-drug and/or drug-food interactions. Review patient medical profile and drug package insert for specific drug and food interactions and recommendations.” This affects the following templates:

- COL14: FOLFIRI (Fluorouracil Continuous Infusion/Leucovorin/Irinotecan) + Bevacizumab
- COL18: Irinotecan Every 21 Days + Cetuximab
- COL19: Irinotecan Every 14 Days + Cetuximab
- COL20: Irinotecan Days 1 and 8 every 21 Days + Cetuximab
- COL22: FOLFIRI (Fluorouracil Continuous Infusion/Leucovorin/Irinotecan) + Cetuximab
- COL32: Irinotecan Every 21 Days
- COL33: Irinotecan Days 1 and 8 Every 21 Days
- COL46: FOLFOXIRI (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin/Irinotecan) + Bevacizumab
- COL47: IROX (Irinotecan/OXALIplatin)
- COL49: FOLFIRI (Fluorouracil Continuous Infusion/Leucovorin/Irinotecan) + Panitumumab

Titles have been changed on the following templates:

- COL20: Irinotecan + Cetuximab changed to Irinotecan Day 1 and 8 Every 21 Days + Cetuximab
- COL33: Irinotecan changed to Irinotecan Days 1 and 8 Every 21 Days

References have been updated on the following templates:

- COL2: mFOLFOX6 (Fluorouracil Continuous Infusion/Leucovorin/OXALIplatin)
- COL42: Capecitabine + Bevacizumab

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Acute Myeloid Leukemia. These NCCN Guidelines® for Acute Myeloid Leukemia are currently available as Version 1.2018.

Evaluation for Acute Leukemia/Diagnosis (AML-1, AML-1A)

- Bullet 6 modified: Molecular analyses (KIT, FLT3 [ITD and TKD], NPM1, CEBPA, IDH1, IDH2, TP53, and other mutations)
Footnote "a" modified: Molecular abnormalities (KIT, FLT3-ITD, NPM1, CEBPA, and other mutations) are important for prognostication in a subset of patients (category 2A) and may guide therapeutic intervention (category 2B) (See AML-A). Multiplex gene panels and sequencing assays are available for the assessment of other molecular abnormalities that have prognostic impact in AML or eligibility for clinical trial. A variety of gene mutations are associated with specific prognoses (category 2A) and may guide medical decision making (category 2B) (See AML-A). Currently, c-KIT, FLT3-ITD, FLT3-TKD, NPM1, CEBPA, IDH1/IDH2, and TP53 are included in this group; however, this field is evolving rapidly. While the above mutations should be tested in all patients, multiplex gene panels and next-generation sequencing analysis may be used to obtain a more comprehensive prognostic assessment (Papaemmanuil E, et al. Genomic classification and prognosis in acute myeloid leukemia. N Engl J Med 2016;374:2209-2221). The information obtained may have prognostic impact in AML, may influence medical decision making regarding consolidation with chemotherapy versus an allogeneic hematopoietic stem cell transplant, or determination for eligibility for clinical trial participation (see Discussion). If a test is not available at your institution, consult pathology prior to performing the marrow evaluation about preserving material from the original diagnostic sample for future testing use at an outside reference lab after full cytogenetic data are available. Circulating blasts from peripheral blood can be used to detect molecular abnormalities in patients with blast counts >1000/mcL if a minimum of 10% involvement by the myeloid neoplasm to prevent false-negative results.

Footnote c modified: The WHO 2016 classification defines acute leukemia as ≥20% blasts in the marrow or blood. In an appropriate clinical setting, a diagnosis of AML may be made with less than 20% in patients with recurrent cytogenetic abnormalities (e.g., the following cytogenetic abnormalities: t(15;17), t(8;21), t(16;16), inv(16). AML evolving from MDS (AML-MDS) is often more resistant to cytotoxic chemotherapy than AML that arises without antecedent hematologic disorder and may have a more indolent course. Some clinical trials designed for high-grade MDS may allow enrollment of patients with AML-MDS.

- Classification (AML-2)
  - Category "Able to tolerate anthracyclines" changed to "No cardiac issues"
  - Category "Not able to tolerate anthracyclines" changed to "Cardiac issues (low ejection fraction [EF] or QTc prolongation)" (also applies to AML-5)

- APL Treatment Induction/Consolidation Therapy (High Risk) (AML-3/AML-3A)
  - Headings added to Preferred Regimens and Other Recommended Regimens (also applies to AML-4)
  - The following regimens were removed:
    - Induction: ATRA 45 mg/m² in divided doses daily until clinical remission + daunorubicin 50 mg/m² x 4 days + cytarabine 200 mg/m² x 7 days (category 1)
    - Consolidation: Arsenic trioxide 0.15 mg/kg/d x 5 days for 5 wks x 2 cycles, then ATRA 45 mg/m² x 7 days + daunorubicin 50 mg/m² x 3 days for 2 cycles (category 1)
    - Induction: ATRA 45 mg/m² in divided doses daily until clinical remission + daunorubicin 60 mg/m² x 3 days + cytarabine 200 mg/m² x 7 days (category 1)
    - Consolidation: Daunorubicin 60 mg/m² x 3 days + cytarabine 200 mg/m² x 7 days x 1 cycle, then cytarabine 1 g/m² every 12 h x 4 days + daunorubicin 45 mg/m² x 3 days x 1 cycles (category 1)
  - Bone marrow assessment modified after induction that includes ATRA + arsenic trioxide: At count recovery, bone marrow at day 28 to document remission before proceeding with consolidation. (also applies to AML-4, AML-5)
Footnote s added: If no evidence of morphologic disease, ATRA and arsenic trioxide can be discontinued to allow for peripheral blood recovery since arsenic trioxide can be associated with significant myelosuppression. If evidence of morphologic disease, continue ATRA and arsenic trioxide and repeat marrow 1 week later. (also applies to AML-4, AML-5A)

Footnote u modified: Premature morphologic and molecular assessment (10–14 marrow) can be misleading; a nadir marrow is not recommended. Patients often remain molecularly positive at the end of induction, even when the marrow shows morphologic remission. The first assessment of molecular remission should not be performed prior to count recovery. For all inductions it is premature to do a marrow any sooner than day 28. Patients may be in cytogenetic remission but with residual molecular positivity at that time. (also applies to AML-4, AML-5A)

APL Treatment Induction/Consolidation Therapy (Low Risk) (AML-4/AML-4A)

The following regimens were added to preferred regimens:
- Induction: ATRA 45 mg/m² in divided doses daily + arsenic trioxide 0.15 mg/kg/d IV + gemtuzumab ozogamicin 9 mg/m² day 1
- Consolidation: Arsenic trioxide 0.15 mg/kg IV daily 5 days/week for 4 weeks every 8 weeks for a total of 4 cycles + ATRA 45 mg/m² for 2 weeks every 4 weeks for a total of 7 cycles. If ATRA or arsenic trioxide discontinued due to toxicity, gemtuzumab ozogamicin 9 mg/m² once every 4–5 weeks until 28 weeks from CR
- Induction: ATRA 45 mg/m² in divided doses daily + arsenic trioxide 0.3 mg/kg IV on days 1–5 of week one and 0.25 mg/kg twice weekly in weeks 2–8 (category 1) + gemtuzumab ozogamicin 6 mg/m² day 1
- Consolidation: ATRA 45 mg/m² for 2 weeks every 4 weeks (or for 2 weeks on 2 weeks off) in consolidation courses 1-4 + arsenic trioxide 0.3 mg/kg IV on days 1–5 of week one in consolidation courses 1-4 and 0.25 mg/kg twice weekly in weeks 2–4 in consolidation courses 1-4 (category 1). If ATRA or arsenic trioxide discontinued due to toxicity, gemtuzumab ozogamicin 9 mg/m² once every 4–5 weeks until 28 weeks from CR.

Footnote r added: Burnett AK, et al. Arsenic trioxide and all-trans retinoic acid treatment for acute promyelocytic leukaemia in all risk groups (AML17): results of a randomised, controlled, phase 3 trial. Lancet Oncol 2015;16:1295-1305. (also applies to AML-5A)


APL Treatment Induction/Consolidation Therapy (High Risk - Cardiac issues: low ejection fraction [EF] or QTc prolongation) (AML-5/AML-5A)

The following regimens added:
- Gemtuzumab added to the first regimen:
- Induction: ATRA 45 mg/m² in 2 divided doses daily + arsenic trioxide 0.15 mg/kg IV daily + gemtuzumab ozogamicin 9 mg/m² day 1
- Consolidation: Arsenic trioxide 0.15 mg/kg IV daily 5 days/week for 4 weeks every 8 weeks for a total of 4 cycles + ATRA 45 mg/m2 for 2 weeks every 4 weeks for a total of 7 cycles. If ATRA or arsenic trioxide discontinued due to toxicity, gemtuzumab ozogamicin 9 mg/m² once every 4-5 weeks until 28 days from CR.
Induction: ATRA 45 mg/m² in divided doses daily + arsenic trioxide 0.3 mg/kg IV on days 1–5 of week one and 0.25 mg/kg twice weekly in weeks 2–8 (category 1) + gemtuzumab ozogamicin 6 mg/m² day 1

Consolidation: ATRA 45 mg/m² for 2 weeks every 4 weeks (or for 2 weeks on 2 weeks off) in consolidation courses 1–4 + arsenic trioxide 0.3 mg/kg IV on days 1–5 of week one in consolidation courses 1–4 and 0.25 mg/kg twice weekly in weeks 2–4 in consolidation courses 1–4 (category 1). If ATRA or arsenic trioxide discontinued due to toxicity, gemtuzumab ozogamicin 9 mg/m² once every 4–5 weeks until 28 weeks from CR.

Induction: ATRA 45 mg/m² in 2 divided doses daily + gemtuzumab ozogamicin 9 mg/m² day 1. (For patients not able to tolerate arsenic trioxide for reasons including prolonged QTc)

Consolidation: ATRA 45 mg/m² in divided doses daily during weeks 1–2, 5–6, 9–10, 13–14, 17–18, 21–22, 25–26. Gemtuzumab ozogamicin 9 mg/m² monthly until 28 weeks from CR.


Therapy for APL Relapse (AML-7)

No prior exposure to arsenic trioxide combined with early relapse (<6 mo) after ATRA + anthracycline-containing regimen. Gemtuzumab added as a possible combination with arsenic trioxide ± ATRA.

Late relapse (≥6 mo) after arsenic-trioxide-containing regimen. Gemtuzumab or anthracycline added as possible combination options with arsenic trioxide ± ATRA.

Early relapse (<6 mo) after ATRA and arsenic trioxide (no anthracycline): recommendation changed from "ATRA + idarubicin + arsenic trioxide" to any of the anthracycline-based regimens noted on AML-4 for high-risk APL.

"Consider" added to CNS prophylaxis with IT chemotherapy.

Footnote ii added: Document molecular panel to verify relapsed APL versus therapy-related AML.

AML Treatment Induction (Age <60 y) (AML-8/AML-8A)

The following induction regimens were added:

- Dual-drug liposomal encapsulation of cytarabine 100 mg/m² and daunorubicin 44 mg/m² IV over 90 min on days 1, 3, and 5 (cytotoxic therapy-related AML other than core binding factor [CBF]/APL, or patients with antecedent MDS/CMML, or cytogenetic changes that are consistent with MDS) (category 2B)
- Standard-dose cytarabine 200 mg/m² continuous infusion x 7 days with daunorubicin 60 mg/m² and gemtuzumab ozogamicin 3 mg/m² (up to one 4.5 mg vial) on days 1, 4, and 7 (CD33-positive)


Footnote zz added: Patients with AML and core binding factor (CBF) abnormalities may benefit from the addition of gemtuzumab ozogamicin. Consider screening with FISH to identify abnormalities.
• AML After Standard-Dose Cytarabine Induction (Age <60 y) (AML-9/AML-9A)
  o The following regimen was added for significant residual disease without a hypocellular marrow:
    ▪ Dual-drug liposomal encapsulation of cytarabine 100 mg/m² and daunorubicin 44 mg/m² IV over 90 min on days 1 and 3 for subsequent cycles of induction (cytotoxic therapy-related AML other than CBF/APL, or patients with antecedent MDS/CML, or cytogenetic changes that are consistent with MDS)
  o Footnote eee modified: Hypoplasia is defined as cellularity less than 10%–20% of which the residual blasts are less than 5%–10% (ie, blast percentage of residual cellularity). (also applies to AML-10, AML-13A)
  o Footnote kkk modified: Screening LP should be considered at first remission before first consolidation for patients with monocytic differentiation, mixed phenotype acute leukemia, WBC >40,000/mcL at diagnosis, extramedullary disease, or FLT3. (also applies to AML-10)
• AML Post-Remission Therapy (Age <60 y) (AML-11)
  o Dosing schedule for HiDAC modified to include administration on days 1, 2, 3.
  o Core binding factor (CBF) cytogenetic translocations without KIT mutation or favorable-risk molecular abnormalities
    ▪ The following post-remission regimen added:
      • Cytarabine 1000 mg/m² every 12 hours on days 1–4 + daunorubicin 60 mg/m² on day 1 (first cycle) or days 1–2 (second cycle) + gemtuzumab ozogamicin 3 mg/m² (up to one 4.5 mg vial) on day 1 x 2 cycles (CD33-positive)
  o Intermediate-risk cytogenetics and/or molecular abnormalities
    ▪ HiDAC dosing changed to 1.5-3 g/m²
    ▪ The following post-remission regimen added:
      • Cytarabine 1000 mg/m² every 12 hours on days 1–4 + daunorubicin 60 mg/m² on day 1 (first cycle) or days 1–2 (second cycle) + gemtuzumab ozogamicin 3 mg/m² (up to one 4.5 mg vial) on day 1 x 2 cycles (CD33-positive)
  o Treatment-related disease other than CBF and/or poor-risk cytogenetics and/or molecular abnormalities
    ▪ HiDAC dosing changed to 1.5-3 g/m²
    ▪ The following post-remission regimen added:
      • HIDAC 1.5-3 g/m² over 3 h every 12 h on days 1, 3, 5 or 1, 2, 3 x 3–4 cycles
      • Dual-drug liposomal encapsulation cytarabine 65 mg/m² and daunorubicin and 29 mg/m² IV over 90 min on days 1 and 3 (cytotoxic therapy-related AML or patients with antecedent MDS/CML or cytogenetic changes that are consistent with MDS)
• AML Treatment Induction (Age ≥60 y) (AML-12/AML-12A)
  o Candidate for intensive remission induction therapy
    ▪ De novo AML without unfavorable cytogenetics/molecular markers/No antecedent hematologic disorder/No therapy-related AML
      • The following induction regimens added:
        o Standard dose cytarabine 200 mg/m² continuous infusion x 7 days with daunorubicin 60 mg/m² x 3 days and oral midostaurin 50 mg every 12 hours, days 8-21 (FLT3-mutated AML)
        o Standard-dose cytarabine 200 mg/m² continuous infusion x 7 days with daunorubicin 60 mg/m² and gemtuzumab ozogamicin 3 mg/m² (up to one 4.5 mg vial) on days 1, 4, and 7 (CD33-positive)
    ▪ Unfavorable cytogenetic/molecular markers/Antecedent hematologic disorder/Therapy-related AML
      • The following induction regimen added:
Dual-drug liposomal encapsulation of cytarabine 100 mg/m² and daunorubicin 44 mg/m² IV over 90 min on days 1, 3, and 5 (cytotoxic therapy-related AML or patients with antecedent MDS/CMML or cytogenetic changes that are consistent with MDS) (category 1)

- "Clofarabine ± standard dose cytarabine" changed to "Clofarabine-based regimens" and moved to footnote sss.
- Not a candidate for intensive remission induction therapy or declines intensive therapy
- The following induction regimens were added:
  - Gemtuzumab ozogamicin 6 mg/m² on day 1 and 3 mg/m² on day 8 (CD33-positive)
  - Enasidenib (IDH-2 mutated AML)

- AML After Standard-Dose Cytarabine Induction (Age ≥60 y) (AML-13)
  - The following regimen was added for residual disease: Dual-drug liposomal encapsulation of cytarabine 100 mg/m² and daunorubicin 44 mg/m² IV over 90 min on days 1 and 3 for subsequent cycles, if needed. (cytotoxic therapy-related AML or patients with antecedent MDS/CMML or cytogenetic changes that are consistent with MDS)

- AML Post-Remission Therapy (Age ≥60 y) (Previous intensive therapy) (AML-14/AML-14A)
  - Complete response
    - The following post-remission regimens were added:
      - Dual-drug liposomal encapsulation cytarabine 65 mg/m² and daunorubicin and 29 mg/m² IV over 90 min on days 1 and 3 (cytotoxic therapy-related AML or patients with antecedent MDS/CMML or cytogenetic changes that are consistent with MDS)
      - Cytarabine 1000 mg/m² every 12 hours on days 1–4 + daunorubicin 60 mg/m² on day 1 (first cycle) or days 1–2 (second cycle) + gemtuzumab ozogamicin 3 mg/m² (up to one 4.5 mg vial) on day 1 x 2 cycles (CD33-positive).
    - Maintenance therapy with hypomethylating regimens (5-azacytidine, decitabine) every 4–6 weeks until progression (if patient received hypomethylating agents in induction)
    - Footnote dddd added: An option for patients who had achieved a remission with a more intensive regimen but had regimen related-toxicity that prevented them from receiving more conventional consolidation.

- AML Post-Remission Therapy (Age ≥60 y) (Previous lower intensity therapy) (AML-15)
  - The following regimens added for responding disease:
    - Gemtuzumab ozogamicin 2 mg/m² on day 1 every 4 weeks up to 8 continuation courses (CD33-positive).
    - Continue enasidenib until progression (IDH-2 mutated AML)
  - Footnote eeee added: Response to treatment with enasidenib may take 3-5 months.
Footnote ffff added: Enasidenib increases the risk for differentiation syndrome and hyperleukocytosis that may require treatment with hydroxyurea and steroids.

- Risk Status Based on Validated Cytogenetics and Molecular Abnormalities (AML-A)
  - Molecular Abnormalities
    - Favorable-risk: added "or presence of FLT3-ITD\textsubscript{low}"
    - Intermediate-risk: added "Mutated NPM1 and FLT3-ITD\textsubscript{high} or with FLT3-ITD\textsubscript{low} (without poor-risk genetic lesions)"; removed "+8 alone"
    - Poor-risk: added "Mutated RUNX19"; "Mutated ASXL19"; "Wild-type NPM1 and FLT3-ITD\textsubscript{high}"
    - Footnote 7 added: Low allelic ratio (<0.5). High allelic ratio (≥0.5).
    - Footnote 9 added: These markers should not be used as poor-risk prognostic marker if they co-occur with favorable-risk AML subtypes.

- Response Criteria Definitions for Acute Myeloid Leukemia (AML-D)
  - Last bullet added: Induction failure - Failure to attain CR following exposure to at least 2 courses of intensive induction therapy (2 cycles of 7+3 or one cycle of 7+3 and one cycle of HiDAC).

- Therapy for Relapsed/Refractory Disease (AML-F)
  - Clinical trial added
  - Category added: Therapy for AML with IDH-2 mutation
    - The following regimen was added: Enasidenib
  - Category added: Therapy for CD33-positive AML
    - The following regimen was added: Gemtuzumab ozogamicin
  - Footnote 1 modified with addition of sentence: Molecular profiling should be considered if not done at diagnosis.

The following NCCN Chemotherapy Order Templates (NCCN Templates\textsuperscript{®}) have been deleted to reflect the NCCN Guidelines for Acute Myeloid Leukemia, Version 1.2018.

- Induction: Low risk or Intermediate risk
  - APL14: French-Belgian-Swiss APL 2000 - Induction – Tretinoin (ATRA)/DAUNOrubicin/Cytarabine
• Consolidation: Low risk or Intermediate risk
  o APL15: French-Belgian-Swiss APL 2000 - Consolidation 1 – DAUNOribcin/Cytarabine
  o APL16: French-Belgian-Swiss APL 2000 - Consolidation 2 – DAUNOribcin/High-Dose Cytarabine

February 5, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Ovarian Cancer. These NCCN Guidelines® are currently available as Version 5.2017.

• Monitoring/follow-up for stage I-IV disease following complete response to primary therapy (OV-5)
  o Tumor molecular testing has been added to the follow-up recommendations if rising CA-125 and/or clinical relapse occurs during monitoring/follow-up for recurrent disease.
  o Footnote "w" has been added: “Validated molecular testing should be performed in a CLIA-approved facility using the most recent available tumor tissue. Testing should include at least: BRCA 1/2, homologous recombination pathway genes, and microsatellite instability or DNA mismatch repair.” (Also on OV-6)

• Acceptable Recurrence Therapies for Epithelial (including LCOH)/Fallopian Tube/Primary Peritoneal Cancer Options OV-B (6 of 8)
  o The following targeted therapy has been added to the list of other potentially active recurrence therapy options: Pembrolizumab (category 2A) (for microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] solid tumors) (Varga A, Piha-Paul SA, Ott PA, et al. Pembrolizumab in patients (pts) with PD-L1–positive (PD-L1+) advanced ovarian cancer: Updated analysis of KEYNOTE-028 [abstract]. J Clin Oncol 2017;35: Abstract 5513.)

*For your reference, the previous update (Version 4.2017) to the NCCN Guidelines for Ovarian Cancer, published on November 9, 2017 is available at the following link:

NCCN has published updates to the following NCCN Guidelines with NCCN Evidence Blocks™:

• Bladder Cancer, Version 1.2018
• Penile Cancer, Version 1.2018
January 26, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), NCCN Drugs & Biologics Compendium (NCCN Compendium®), and the NCCN Radiation Therapy Compendium™ for Thymomas and Thymic Carcinomas. These NCCN Guidelines® are currently available as Version 1.2018.

- **Initial Evaluation (THYM-1)**
  - Thymic tumor unlikely: Consider tissue biopsy added.

- **Principles of Surgical Resection (THYM-A)**
  - Bullet 7 is new to the page: Surgical clips should be placed at the time of resection to areas of close margins, residual disease, or tumor adhesion to unresected normal structures to help guide accurate radiation therapy when indicated.

- **Principles of Radiation Therapy (THYM-B 1 of 3)**
  - **General Principles**
    - Bullet 4 modified: The review of preoperative imaging and co-registration of preoperative imaging into the planning system may be helpful in defining treatment volumes.
  - **Radiation Doses**
    - Last bullet added: Depending on the treatment objectives in the palliative setting, typical palliative doses (e.g., 8 Gy single fraction, 20 Gy in 5 fractions, 30 Gy in 10 fractions) up to definitive doses for more durable local control and highly conformal techniques for limited volume metastases may be appropriate, given the relatively long natural history of even metastatic thymoma.

- **Principles of Chemotherapy (THYM-C)**
  - VIP regimen name replaced with “Etoposide/Ifosfamide/Cisplatin.”

- **WHO Classification information has been updated (THYM-D)**


NCCN has published NCCN Chemotherapy Order Templates (NCCN Templates®) for Colon Cancer to reflect the currently published NCCN Guidelines for Colon Cancer, Version 1.2018.

- The following NEW NCCN Templates® have been published:
  - COL50: Regorafenib
  - COL51: Irinotecan + Panitumumab
  - COL52: FOLFIRI (Fluorouracil Continuous Infusion/Leucovorin/Irinotecan) + Ziv-aflibercept
  - COL53: Irinotecan + Ziv-aflibercept
  - COL54: Irinotecan + Bevacizumab
  - COL55: IROX (OXALIplatin/Irinotecan) + Bevacizumab
  - COL57: FOLFOXIRI (Fluorouracil Continuous Infusion/OXALIplatin/Irinotecan) + Bevacizumab
  - COL58: Irinotecan Every 14 Days
NCCN has published updates to the NCCN Templates for Testicular Cancer to reflect the currently published NCCN Guidelines for Testicular Cancer, Version 1.2018.

- The following NEW NCCN Template has been published:
  - TES14: Pembrolizumab

- Indications for all testicular cancer templates have been revised to be more specific.

  - TES10: Gemcitabine/PACLitaxel

- Cycle information for the following template has been revised to “21-day cycle for 4 cycles (primary: seminoma) or 2 – 4 cycles (primary: nonseminoma) or 2 cycles (residual: seminoma or residual: nonseminoma)”
  - TES5: EP (CISplatin/Etoposide)

- The following note for regimens with a high risk of febrile neutropenia has been updated in the Myeloid Growth Factor Therapy section: “Filgrastim or tbo-filgrastim or filgrastim-sndz 5 mcg/kg subcutaneously daily recommended to start the day following or up to 3 – 4 days after completion of chemotherapy and to continue until post-nadir ANC recovery to normal or near-normal levels by laboratory standards. Dose is rounded to the nearest vial size by institution-defined weight limits. Same-day administration is not recommended. OR Pegfilgrastim 6 mg subcutaneously once per treatment cycle recommended to be given the day following or up to 3 – 4 days after completion of chemotherapy. There are insufficient data to support use of pegfilgrastim for cytotoxic chemotherapy regimens administered less frequently than every 2 weeks. Same-day administration is not recommended.”
  - TES1: BEP (Bleomycin/Etoposide/CISplatin)
  - TES3: TIP (PACLitaxel/Ifosfamide/CISplatin)
  - TES6: VelP (VinBLAStine/Ifosfamide/Mesna/CISplatin)
  - TES9: VIP (Etoposide/Ifosfamide/Mesna/CISplatin)

- The following NEW note for CARBOplatin has been added to the Monitoring and Hold Parameters section: “Electrolytes (eg, magnesium, potassium) should be monitored as clinically indicated.”
  - TES7: CARBOplatin

- The following NEW note for CARBOplatin, CISplatin, PACLitaxel, and vinBLAStine has been added to the Monitoring and Hold Parameters section: “This agent may cause peripheral neuropathy. Monitor patients as
clinically indicated for persistent issues with altered sensation including pain or discomfort and/or regional motor weakness that may interfere with activities of daily living. Dose modification or discontinuation of therapy may be warranted.

- TES1: BEP (Bleomycin/Etoposide/CISplatin)
- TES3: TIP (PAACLitaxel/Ifosfamide/CISplatin)
- TES5: EP (CISplatin/Etoposide)
- TES6: VelP (VinBLAStine/Ifosfamide/Mesna/CISplatin)
- TES7: CARBOplatin
- TES9: VIP (Etoposide/Ifosfamide/Mesna/CISplatin)
- TES10: Gemcitabine/PAACLitaxel
- TES11: Gemcitabine/PAACLitaxel/OXALIplatin

- The following note for CISplatin and PAACLitaxel has been deleted from the Monitoring and Hold Parameters section: “Signs and symptoms of neurotoxicity should be monitored as clinically indicated for potential dose modification or discontinuation.” (replaced with the more specific peripheral neuropathy note above)

- TES3: TIP (PAACLitaxel/Ifosfamide/CISplatin)
- TES10: Gemcitabine/PAACLitaxel
- TES11: Gemcitabine/PAACLitaxel/OXALIplatin

- The following NEW note for gemcitabine has been added to the Safety Parameters and Special Instructions section: “This agent is an irritant.”

- TES10: Gemcitabine/PAACLitaxel
- TES11: Gemcitabine/PAACLitaxel/OXALIplatin

- The following note for PAACLitaxel has been updated in the Safety Parameters and Special Instructions section: “This agent should be prepared either in glass or non-PVC containers and administered through non-PVC tubing and a low protein binding 0.2 or 0.22 micron in-line filter.”

- TES3: TIP (PAACLitaxel/Ifosfamide/CISplatin)
- TES10: Gemcitabine/PAACLitaxel
- TES11: Gemcitabine/PAACLitaxel/OXALIplatin

- The following NEW notes for vinBLAStine have been added to the Safety Parameters and Special Instructions section: “VinBLAStine is for IV use only and usually results in death or serious neurological damage if given via other routes,” and “VinBLAStine should be administered via a minibag (eg, 25 mL – 50 mL).”

- TES6: VelP (VinBLAStine/Ifosfamide/Mesna/CISplatin)

NCCN has published updates to the NCCN Templates for Uterine Neoplasms to reflect the currently published NCCN Guidelines for Uterine Neoplasms. Version 1.2018.

- The following NEW NCCN Templates have been published:
  - UTE17: Everolimus + Letrozole
  - UTE18: Albumin-bound PAACLitaxel
  - UTE19: Pembrolizumab
  - UTS17: Trabectedin
  - UTS18: DOXOrubicin + Olaratumab
• Indications and cycle information for all endometrial carcinoma and uterine sarcoma templates have been revised.

• References have been updated on the following templates:
  - UTE4: DOCEtaxel/CARBOplatin
  - UTE5: Liposomal DOXOrubicin
  - UTE6: DOXOrubicin
  - UTE11: PACLitaxel
  - UTS1: Gemcitabine/DOCEtaxel
  - UTS3: Ifosfamide
  - UTS5: Dacarbazine

• The febrile neutropenia risk on template UTE4: DOCEtaxel/CARBOplatin has been updated to “Intermediate”.

• The dosing for template UTE5: Liposomal DOXOrubicin has been updated to a range of 40-50 mg/m².

• A new dosing option has been added to the following templates:
  - UTS3: Ifosfamide
  - UTS5: Dacarbazine

• The following note for regimens with a high risk of febrile neutropenia has been updated in the Myeloid Growth Factor Therapy section: “Filgrastim or tbo-filgrastim or filgrastim-sndz 5 mcg/kg subcutaneously daily recommended to start the day following or up to 3 – 4 days after completion of chemotherapy and to continue until post-nadir ANC recovery to normal or near-normal levels by laboratory standards. Dose is rounded to the nearest vial size by institution-defined weight limits. Same-day administration is not recommended. OR Pegfilgrastim 6 mg subcutaneously once per treatment cycle recommended to be given the day following or up to 3 – 4 days after completion of chemotherapy. There are insufficient data to support use of pegfilgrastim for cytotoxic chemotherapy regimens administered less frequently than every 2 weeks. Same-day administration is not recommended.”
  - UTS2: DOCEtaxel
  - UTS6: DOXOrubicin
  - UTS11: DOXOrubicin/ifosfamide

• The following NEW note for CARBOplatin has been added to the Monitoring and Hold Parameters section: “Electrolytes (eg, magnesium, potassium) should be monitored as clinically indicated.”
  - UTE3: PACLitaxel/CARBOplatin
  - UTE4: DOCEtaxel/CARBOplatin
  - UTE10: CARBOplatin

• The following NEW note for CARBOplatin, CISplatin, DOCEtaxel, eriBULin, PACLitaxel, and vinORELBine has been added to the Monitoring and Hold Parameters section: “This agent may cause peripheral neuropathy. Monitor patients as clinically indicated for persistent issues with altered sensation including pain or discomfort and/or regional motor weakness that may interfere with activities of daily living. Dose modification or discontinuation of therapy may be warranted.”
  - UTE1: DOXOrubicin/CISplatin/PACLitaxel
UTE2: DOXOrubicin/CISplatin
UTE3: PACLitaxel/CARBOplatin
UTE4: DOCEtaxel/CARBOplatin
UTE7: DOCEtaxel
UTE9: CISplatin
UTE10: CARBOplatin
UTE11: PACLitaxel
UTE12: Ifosfamide/PACLitaxel
UTE14: Ifosfamide/CISplatin
UTS1: Gemcitabine/DOCEtaxel
UTS2: DOCEtaxel
UTS14: Gemcitabine/VinORELBine
UTS15: VinORELBine
UTS16: EriBULIn

The following note for CISplatin, DOCEtaxel, eriBULIn, and PACLitaxel has been deleted from the Monitoring and Hold Parameters section: “Signs and symptoms of neurotoxicity should be monitored as clinically indicated for potential dose modification or discontinuation.” (replaced with the more specific peripheral neuropathy note above)
UTE1: DOXOrubicin/CISplatin/PACLitaxel
UTE2: DOXOrubicin/CISplatin
UTE3: PACLitaxel/CARBOplatin
UTE4: DOCEtaxel/CARBOplatin
UTE7: DOCEtaxel
UTE9: CISplatin
UTE11: PACLitaxel
UTE12: Ifosfamide/PACLitaxel
UTE14: Ifosfamide/CISplatin
UTS1: Gemcitabine/DOCEtaxel
UTS2: DOCEtaxel
UTS16: EriBULIn

The following NEW note for dacarbazine has been added to the Monitoring and Hold Parameters section: “Liver function should be monitored prior to initiation of therapy and as clinically indicated for potential dose modification or discontinuation.”
UTS5: Dacarbazine
UTS12: DOXOrubicin/Dacarbazine
UTS13: Gemcitabine/Dacarbazine

The following NEW note for DOCEtaxel has been added to the Monitoring and Hold Parameters section: “This agent may cause changes to fingernails and toenails including color, texture, and shape. This is usually a reversible side effect, but should be monitored throughout treatment.”
UTE4: DOCEtaxel/CARBOplatin
UTE7: DOCEtaxel
UTS1: Gemcitabine/DOCEtaxel
UTS2: DOCEtaxel
• The following NEW note for PAZOPanib has been added to the Monitoring and Hold Parameters section: This agent may cause interstitial lung disease. Monitor for nonspecific respiratory signs and symptoms, including hypoxia, pleural effusion, cough, or dyspnea. Modification or discontinuation of therapy may be warranted.
  o UTS10: PAZOPanib

• The following NEW note for temsirolimus has been added to the Monitoring and Hold Parameters section: “Renal function should be monitored prior to initiation of therapy and as clinically indicated for potential dose modification or discontinuation.”
  o UTE16: Temsirolimus

• The following note for PACLitaxel has been updated in the Safety Parameters and Special Instructions section: “This agent should be prepared either in glass or non-PVC containers and administered through non-PVC tubing and a low protein binding 0.2 or 0.22 micron in-line filter.”
  o UTE1: DOXOrubicin/CISplatin/PACLitaxel
  o UTE3: PACLitaxel/CARBOplatin
  o UTE11: PACLitaxel
  o UTE12: Ifosfamide/PACLitaxel

• The following note for temsirolimus has been updated in the Safety Parameters and Special Instructions section: “This agent should be prepared either in glass or non-PVC containers and administered through non-PVC tubing and a low protein binding ≤5 micron in-line filter.”
  o UTE16: Temsirolimus

• The following NEW note for gemcitabine and topotecan has been added to the Safety Parameters and Special Instructions section: “This agent is an irritant.”
  o UTE15: Topotecan
  o UTS1: Gemcitabine/DOCEtaxel
  o UTS8: Gemcitabine
  o UTS13: Gemcitabine/Dacarbazine
  o UTS14: Gemcitabine/VinORELBine

• The following note for vinORELBine has been updated in the Safety Parameters and Special Instructions section: “VinBLAStine is for IV use only and usually results in death or serious neurological damage if given via other routes.”
  o UTS14: Gemcitabine/VinORELBine
  o UTS15: VinORELBine

NCCN has published updates to the NCCN Biomarkers Compendium®, based on updates to the following NCCN Guidelines:

• Bone Cancer, Version 1.2018
• Cervical Cancer, Version 1.2018
• Genetic/Familial High Risk Assessment: Breast and Ovarian, Version 1.2018
January 24, 2018

NCCN has published the following NEW NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) with NCCN Evidence Blocks™:

- Occult Primary, Version 1.2018

NCCN has published updates to the NCCN Guidelines® for Adult Cancer Pain. These NCCN Guidelines are currently available as Version 1.2018.

- Principles of Cancer Pain Management (PAIN-1)
  - Under “General” a bullet was revised: “Analgesic therapy is often done in conjunction with management of multiple symptoms or symptom clusters. Treatment must consider the interaction of complex pharmacologic therapies that a patient is prescribed and the risk for analgesic misuse.”
  - Under “Management/Intervention”, a bullet for “Goals of pain management” was added: “Affect (relationship between pain and mood).”

- Universal Screening (PAIN-2)
  - Under “Comprehensive pain assessment” two sub-bullets were added:
    - “Pain experience”
    - “Risks for substance use disorder (see PAIN-E)”
  - Under “Management of Pain”
    - A footnote was revised and added to “Opioid tolerant patients” statement: “Opioid naïve includes patients who are those not chronically receiving opioid analgesic on a daily basis and therefore have not developed significant tolerance. Opioid tolerant includes patients who are chronically receiving opioid analgesic on a daily basis. The FDA identifies tolerance as receiving at least 25 mcg/h fentanyl patch, at least 60 mg of morphine daily, at least 30 mg of oral oxycodone daily, at least 8 mg of oral hydromorphone daily, or an equianalgesic dose of another opioid for a week or longer.” (Also for PAIN-3, PAIN-4, PAIN-5 and PAIN-6)

- Management of Pain in Opioid-Naïve Patients (PAIN-3)
° This page was extensively revised.

- Initiating Short-Acting Opioids in Opioid-Naïve Patients (PAIN-4)
  ° Two pathway statements for “Opioid-naïve patients” were revised:
    ▪ "Oral analgesic (peak effect 60 min)"
    ▪ "Oral analgesics require a minimum of 60 min to reach peak effect"

- Subsequent Pain Management (PAIN-6)
  ° This page was extensively revised.

- Ongoing Care (PAIN-7)
  ° For Ongoing care bullets were revised:
    ▪ "Routine follow-up Have regular follow-up schedule to monitor pain therapy outcomes"
    ▪ "Ensure adequate access to prescribed medications, especially continuity of care during transition between sites of care"
      ○ First sub-bullet under this statement was revised: "Collaborate with patient’s pharmacist and insurance company if needed"

- Procedure-Related Pain and Anxiety (PAIN-B)
  ° A bullet under "Anxiolytics" was revised: "Anxiolytics should be given preemptively when feasible. Examples include midazolam if experienced with its administration and provided onsite, or oral lorazepam or alprazolam. Oral anxiolytics should be administered at least 30 minutes before a procedure, up to an hour before. Patients should be cautioned to avoid driving or operating machinery if taking an anxiolytic prior to a procedure."

- "Interventions For Cancer Management Strategies For Specific Cancer Pain Syndromes" title was revised. (PAIN-D)
  ° A statement was revised: “In general, Moderate to severe cancer pain is treated with opioids as indicated on (PAIN-3); these interventions are meant to complement opioid management. Adjuvant analgesics are used depending on the pain diagnosis, comorbidities, and potential for drug interactions. Integrative interventions should also be optimized (See PAIN-J)"
  ° A bullet was added under "Bone pain without oncologic emergency": "Assess for impending fracture with plain radiographs."
  ° Two bullets under "Bowel Obstruction" were revised:
    ▪ "Evaluate etiology of bowel obstruction. If resulting from cancer, consider surgical intervention. Palliative surgery, radiation, and/or chemotherapy for symptomatic bowel obstruction."
    ▪ "For medical management of partial bowel obstruction consider corticosteroids and/or metoclopramide" bullet is new.
  ° The last bullet was revised: "For severe refractory pain in the imminently dying, consider palliative sedation (see NCCN Guidelines for Palliative Care)."

- Opioid Principles, Prescribing, Titration, Maintenance, And Safety (PAIN-E 1 of 12)
  ° Under “General Principles” one bullet was added: "Consider documentation of opioid and controlled substance agreement."
Under “General Principles” two bullets were revised:

- “Monitor for aberrant drug-taking behaviors or evidence of diversion. May include patient survey tool (eg, COMM). See PAIN E (3 of 13). Educate the patients and caregivers about safe use, storage, and disposal of opioids.”
- A bullet was revised: “Be mindful of Use caution when combining opioid medications with other medications that have a sedating effect (eg, benzodiazepines).”

http://www.fda.gov/downloads/drugs/drugsafety/ucm518672.pdf (Also for PAIN-E 6 of 12)

Under “General Principles” two bullets were removed:

- “If opioid dose reduction is desired or indicated consider opioid dose reduction by 50% to 75% with subsequent reevaluation and further dose adjustment.”
- “If patient is experiencing unmanageable adverse effects and pain is ≤3 (mild), consider downward dose titration by approximately 10% to 25% and reevaluate. Close follow-up is required to make sure that the pain does not escalate, and that the patient does not develop symptoms of withdrawal.”

Opioids And Risk Evaluation And Mitigation Strategy (REMS) (PAIN E 2 of 12)

Three bullets about opioid use and misuse were revised:

- “Opioids are the principal analgesics for moderate to severe pain, yet opioids pose risks to patients and society. In 2013-2014 there were 43,982-47,055 drug-poisoning deaths in the United States, including 46,235-28,647 drug-poisoning deaths involving opioid analgesics. The opioid analgesic overdose deaths have plateaued, decreasing between 2011 and 2013; however, Drug poisoning still remains the number one cause of injury-related deaths. Most people who overdose on prescription opioids not prescribed to them have been given (not bought or stolen) opioids from friends or family. See CDC Morbidity and Mortality Weekly Report, Increases in Drug and Opioid-Involved Overdose Deaths—United States, 2010-2015.https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm655051e1.pdf”
- “Responding to the “public health crisis of addiction, misuse, abuse, overdose, and death,” the FDA is in the process of has established REMS programs for all potent opioid products. See Opioid Drugs and Risk Evaluation and Mitigation Strategies (REMS). Provider and patient education are the principal recommendations of proposed opioid REMS programs.”
- “Make use of state PDMPs if available. The National Association of State Controlled Substances Authorities (http://www.nasca.org/index.htm) maintains a database of state PDMP contacts.”

“Principles of Opioid Dose Reduction” is a new page to the guideline. (PAIN-E 5 of 13)

Strategies to Maintain Patient Safety and Minimize the Risk of Opioid Misuse and Abuse During Chronic Opioid Use (PAIN E 6 of 12)

- “Risk Assessment”
  - A bullet was revised: “Risk assessment prior to and during treatment is recommended, using assessment tools with adequate predictive validity and reliability although current assessment tools have not been validated in the setting of cancer care and clinical judgment should be exercised.
  - A bullet was added: “Comprehensive psychological evaluation can be helpful in assessing risk for substance use disorders.”
- Under “Support for high-risk patients” 3 bullets were added:
  - “Consider referral to multidisciplinary team including an addiction specialist.”
  - “Consider utilizing programmable, electronic medication dispensers.”
"Consider earlier referral to interventional pain specialist to maximize non-opioid options for pain control."

Under "Support for high-risk patients" 2 bullets were revised:
- "Ensure education of caregivers in the proper indications and usage of naloxone. [https://www.samhsa.gov/capt/tools-learning-resources/opioid-overdose-prevention-toolkit]"
- "Pill counts may be used at outpatient visits or by home health/hospice to assist in correct use of medication and verify the information documented in the pain medication diary."

Oral and Parenteral Opioid Equivalences and Relative Potency of Drugs as Compared with Morphine Based on Single-Dose Studies (PAIN-E 7 of 13)
- Opioid Agonists
  - Fentanyl parental dose was added: "0.1 mg"
  - Tramadol
    - Parental dose was added: "100 mg"
    - Oral dose was added: "300 mg"
    - Factor (IV to PO) was added: "3"
    - A footnote was added: "The manufacturer recommends a maximum single dose of tramadol not to exceed 100 mg, with a maximum daily dose of 400 mg for IR formulations (300 mg/d in older adults, 200 mg/d for renal impairment) or 300 mg/d for ER formulations."
- Tapentadol
  - Oral dose was added: "75–100 mg."
  - A footnote was added: "The maximum daily dose for tapentadol ER is 500 mg, or 600 mg IR (lower doses are recommended for moderate hepatic impairment, avoid with severe impairment)."

Miscellaneous Analgesics (PAIN-E 8 of 13)
- A statement about "Partial agonists" was revised: "Transdermal buprenorphine, a partial mu-agonist, has been approved for chronic pain. Although experience with this drug in the management of cancer pain is limited, anecdotal reports, a few small prospective uncontrolled studies, and at least one randomized trial support its use in cancer-related pain. Buprenorphine patch at lowest dose (5 mcg/h) may be used in opioid-naive patients requiring initiation of long-acting opioid therapy. Because buprenorphine is a partial mu-receptor agonist, it exhibits a ceiling to analgesic efficacy and may precipitate withdrawal symptoms if administered to individuals currently taking a high-dose opioid. FDA guidelines recommend limiting dose to 20 mcg per hour due to concern for QT prolongation. Conversion to buprenorphine from other opioids may be complex; consider a pain specialty consultation."
- A bullet under "Non-opioid analgesic" was added: "Intravenous lidocaine infusion may be a useful therapy for refractory pain."

Dose Conversion Ratios for Total 24-hour Oral Morphine to Oral Methadone (PAIN-E 13 of 13)
- A statement was revised: "Note: If the total daily dose equivalent of morphine is greater than 400 mg, a higher dose ratio is necessary and dose titration is recommended. a pain or palliative care specialist should be consulted."

Management of Opioid Adverse Effects (PAIN-F 1 of 3)
- Two bullets were added under "Constipation: Preventative Measures"
- “Educate patient and family on the need for bowel movements despite minimal intake of food.”
- “Set goals of treatment and explain to patient and family (eg, soft stool, ease of defecation, bowel movement every 2 days or less).

  A bullet was revised under “If constipation persists”: “When response to laxative therapy has not been sufficient for opioid-induced constipation in patients with advanced illness, consider oral methylnaltrexone or naloxegol (FDA approved for opioid-induced constipation).”

- Management of Opioid Adverse Effects (PAIN-F 2 of 3)
  - A bullet under “If nausea develops” was revised: “As an alternative, serotonin antagonists should be considered due to lower risk of CNS adverse effects (eg, ondansetron, 4–8 mg PO 3 times daily oral tablet or orally disintegrating tablet; granisetron, 2 mg PO daily). Use with caution as constipation is an adverse effect. Also consider alternative agents such as scopolamine, dronabinol, or olanzapine for nausea management.”

- Adjuvant Analgesics For Neuropathic Pain (Antidepressants, Anticonvulsants, Topical Agents, and Corticosteroids) (PAIN-G 2 of 2)
  - A bullet for “TCAs (eg, amitriptyline, imipramine, nortriptyline, desipramine)” was added: “TCAs should be used with caution in patients with conduction abnormalities or ischemic heart disease”
  - A bullet for “Anticonvulsants examples” was revised: “Pregabalin- Starting dose 50–25 mg nightly, with increasing dose frequency, to 2-3 times a day, and increasing dose increments of 50%–100% every 3 days three times a day to a maximum daily dose of increase to 100 600 mg. times a day. Slower titration for the elderly or medically frail. Dose adjustment required for those with renal insufficiency. Pregabalin is more efficiently absorbed through the GI tract than gabapentin. May increase further to a maximum dose of 600 mg in divided doses 2-3 times a day.”

- Non-Opioid Analgesic (Nonsteroidal Anti-Inflammatory Drugs [NSAIDS] and Acetaminophen) Prescribing (PAIN-K 1 of 2)
  - Under “NSAIDS” a bullet was revised: “The FDA warns that long-term use of NSAID use increases the risk of heart attack or stroke.”
  - Cardiac toxicities (PAIN-K 2 of 2)
    - A bullet was added: “The use of concomitant NSAID with prophylactic aspirin may reduce the effectiveness of aspirin. Therefore, it is recommended to either avoid use or take separately to avoid this possibility.”
    - A bullet was revised: “Treatment: discontinue NSAID if congestive heart failure or hypertension develops or worsens. Naproxen and ibuprofen are preferred NSAIDs for individuals at high risk for cardiac toxicities. All NSAIDs have been associated with cardiac toxicities.”

- The Discussion section has been updated to reflect the changes to the algorithm. (MS-1)

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Myeloid Leukemia. These NCCN Guidelines® are currently available as Version 4.2018.

- Based on the recent FDA updates regarding nilotinib discontinuation, the criteria for discontinuation of TKI therapy and recommendations for post-discontinuation monitoring were revised.
Discontinuation of TKI Therapy (CML-E)

Criteria for discontinuation

- Bullet removed: No history of resistance to any TKI.
- Bullet 6 modified: Access to a reliable qPCR test with a sensitivity of detection at least MR4.5 (BCR-ABL1 ≤ 0.0032% IS) of ≥4.5 logs that reports results on the IS and provides results within 2 weeks.
- Bullet 7 modified: Monthly molecular monitoring for one year, then every 6 weeks for the second year, and every 12 weeks thereafter the first six months following discontinuation, bimonthly during months 7–24, and quarterly thereafter (indefinately) is recommended for patients who remain in MMR (MR3; BCR-ABL1 ≤0.1% IS) after discontinuation of TKI therapy.
- Bullet 8 modified: Prompt resumption of TKI within 4 weeks of a loss of MMR with a monthly molecular monitoring every 4 weeks until MMR is re-established, then every 12 weeks thereafter for the first six months following resumption of TKI and every 3 months thereafter is recommended indefinitely for patients who have reinitiated TKI therapy after a loss of MMR. For those who fail to achieve MMR after three six months of TKI resumption, BCR-ABL1 kinase domain mutation testing should be performed, and monthly molecular monitoring should be continued for another six months.

The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

*For your reference, the previous update (Version 3.2018) to the NCCN Guidelines for Chronic Myeloid Leukemia, published on December 20, 2017, is available at the following link: https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf

January 23, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Melanoma. These NCCN Guidelines® are currently available as Version 2.2018.

- Principles of Sentinel Lymph Node Biopsy (SLNB) (ME-E)
  - This is a new section that provides general principles for performing SLNB, including recommendations for application of nuclear medicine, surgical, and pathology techniques.

- Principles of Radiation Therapy for Melanoma (ME-G)
  - This section was extensively revised to clarify clinical context and include recommended radiation dosing and modalities.

- Systemic Therapy for Metastatic or Unresectable Disease (ME-H)
  - First-line therapy: Nivolumab/ipilimumab changed from category 2A to category 1.

*For your reference, the previous update (Version 1.2018) to the NCCN Guidelines for Melanoma, published on
January 22, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Related Fatigue. These NCCN Guidelines® are currently available as Version 1.2018.

- Standards of Care for Cancer-Related Fatigue in Children/Adolescents and Adults (FT-2)
  - Bullet revised: "Implementation of guidelines for fatigue evaluation and management is best accomplished by interdisciplinary teams who are able to tailor interventions to the needs of the individual patient. Consider referral to an appropriate specialist or supportive care provider (e.g., survivorship, palliative care, integrative oncology, psychology, psychiatry, physical therapy)."

- Screening (FT-3)
  - Management recommendation modified: “Education, counseling, and general strategies for management of fatigue with an emphasis on continued surveillance.”

- Assessment of Treatable Contributing Factors (FT-4)
  - “Vitamin status” is a new addition to nutritional deficits/imbalance.

- General Strategies for Management of Fatigue (FT-5)
  - For patients under active treatment, post treatment, and at end-of-life, these recommendations have been moved to a separate page.

- Interventions for Patients on Active Treatment (FT-6)
  - Physical activity recommendation revised: “Consider initiation and/or encourage maintenance of an exercise program, as appropriate per health care provider, consisting of both endurance (walking, jogging, or swimming) and resistance (weights) training.” (also for patients post-treatment)

January 19, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer. These NCCN Guidelines® are currently available as Version 2.2018.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

*For your reference, the previous update (Version 1.2018) to the NCCN Guidelines for Small Cell Lung Cancer, published on September 21, 2017, is available at the following link: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf*
NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Lung Cancer Screening. These NCCN Guidelines® are currently available as Version 3.2018.

- Follow-up of Screening Findings (LCS-3, LCS-4, LCS-7, LCS-8)
  - Footnote q modified: Criteria for suspicion of malignancy: hypermetabolism higher than the background of surrounding lung parenchyma greater than the adjacent mediastinal blood pool, regardless of absolute SUV.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

*For your reference, the previous update (Version 2.2018) to the NCCN Guidelines for Lung Cancer Screening, published on August 9, 2017, is available at the following link: https://www.nccn.org/professionals/physician_gls/pdf/lung_screening.pdf

NCCN has published updates to the NCCN Guidelines and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Colon Cancer and Rectal Cancer. These NCCN Guidelines for Colon Cancer are currently available as Version 1.2018. The NCCN Guidelines for Rectal Cancer are currently available as 4.2017.

- Adjuvant Treatment (COL-3)
  - Stage III colon cancer treatment recommendations differentiated based on risk status
    - Low-risk stage III is defined as T1-3, N1
      - Preferred treatment recommendations include: CAPEOX for 3 months or FOLFOX for 3–6 months [category 1 for 6 months]
      - Other treatment options include: Capecitabine or 5-FU for 6 months
    - High-risk stage III is defined as T4, N 1-2; T any, N2
      - Preferred treatment recommendations include: CAPEOX for 3–6 months [category 1 for 6 mo] or FOLFOX for 6 months (category 1)
      - Other treatment options include: Capecitabine or 5-FU for 6 months

  - Footnote r added: “In patients staged as T1-3, N1 (low-risk stage III), 3 months of CAPEOX is non-inferior to 6 months of CAPEOX for disease-free survival; non-inferiority of 3 vs. 6 months FOLFOX has not been proven. In patients staged as T4, N 1-2 or T any, N2 (high-risk stage III), 3 months of FOLFOX is inferior to 6 months of FOLFOX for disease-free survival, whereas non-inferiority of 3 vs. 6 months CAPEOX has not been proven. Grade 3+ neurotoxicity rates are lower for patients who receive 3 months vs. 6 months of treatment (3% vs. 16% for FOLFOX; 3% vs. 9% for CAPEOX). Shi Q, et al. J Clin Oncol 2017;35 (suppl):LBA1.”

- Workup of metastatic disease (COL-4, REC-6, REC-7, REC-9, REC-11)
  - Bullet 5 modified: “Determination of tumor gene status for RAS (KRAS and NRAS) and BRAF (individually or as part of next-generation sequencing [NGS] panel)” (COL-4)
  - Footnote t modified: Determination of tumor gene status for RAS (KRAS and NRAS) and BRAF (individually or as part of next-generation sequencing [NGS] panel). (REC-6, REC-7, REC-9, REC-11)
• Unresectable metachronous metastases (COL-11, REC-11)
  o Primary treatment
    ▪ Previous adjuvant FOLFOX/CAPEOX within past 12 months
    ▪ The following regimen was added: "(Irinotecan + [cetuximab or panitumumab] + vemurafenib [BRAF V600E mutation positive])"
    ▪ Footnote modified: "BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor."

• Principles of Imaging section added. (COL-A)

• Principles of Pathologic Review (COL-B 4 of 5, REC-B 5 of 6)
  o KRAS, NRAS, and BRAF Testing
    ▪ Bullet 1 modified: "All patients with metastatic colorectal cancer should have tumor tissue genotyped for RAS (KRAS and NRAS) and BRAF mutations. Patients with any known KRAS mutation (exon 2, 3, 4 or non-exon 2) or NRAS mutation (exon 2, 3, 4) should not be treated with either cetuximab or panitumumab. BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor."
  o Microsatellite Instability (MSI) or Mismatch Repair (MMR) Testing
    ▪ Bullet 5 added: "Testing for MSI may be accomplished with a validated NGS panel, especially in patients with metastatic disease who require genotyping of RAS and BRAF."
    ▪ Footnote * modified: "IHC for MMR and PCR DNA analysis for MSI are different assays measuring the same biological effect.

• Continuum of Care – Systemic Therapy for Advanced or Metastatic Disease
  o Subsequent Therapy (COL-D 2 of 10, REC-E 2 of 10)
    ▪ The following regimen was added: "Irinotecan + (cetuximab or panitumumab) + vemurafenib (BRAF V600E mutation positive)" (also applies to COL-D/REC-E 3 of 10, 4 of 10, 5 of 10)
  o Regimens added (COL-D/REC-E) 9 of 10:
    ▪ Irinotecan + cetuximab + vemurafenib (BRAF V600E mutation positive): Irinotecan 180 mg/m² IV every 14 days and cetuximab 500 mg/m² IV every 14 days with vemurafenib 960 mg PO twice daily (reference added to COL-D/REC-E 10 of 10)
    ▪ Irinotecan + panitumumab + vemurafenib (BRAF V600E mutation positive): Irinotecan 180 mg/m² IV every 14 days and panitumumab 6 mg/kg IV over 60 minutes every 2 weeks with vemurafenib 960 mg PO twice daily
    ▪ Pembrolizumab 200 mg every 3 weeks

• Principles of Radiation Therapy (COL-E)
  o Bullet 4 added: Image-guided radiation therapy (IGRT) with kilovoltage (kV) imaging and cone-beam CT imaging should be routinely used during the course of treatment with IMRT and SBRT.

• Principles of Survivorship (COL-H 1 of 2)
  o Management of Late/Long-Term Sequelae from Disease or Treatment
    ▪ Bullet 1 added: “For issues related to distress, pain, neuropathy, fatigue, or sexual dysfunction, see NCCN Guidelines for Survivorship”
    ▪ Bullet 2, sub-bullet 2 added
      ▪ Management of an ostomy
Consider participation in an ostomy support group or coordination of care with a health care provider specializing in ostomy care (i.e. ostomy nurse)

- Screen for distress around body changes (See NCCN Guidelines for Distress Management) and precautions around involvement with physical activity (see page SPA-A in the NCCN Guidelines for Survivorship)
  - Bullet 3; sub-bullet added for oxaliplatin-induced neuropathy
  - Consider non-pharmacologic therapies, such as, heat, ice, or acupuncture
  - Counseling Regarding Healthy Lifestyle and Wellness
    - Bullet 1 added: “Undergo all age and gender-appropriate cancer and preventive health screenings as per national guidelines”
    - Bullet 5 modified: “Consider low-dose daily aspirin 325 mg for secondary prevention.”
    - Bullet 6 modified: “Eliminate or limit alcohol consumption, no more than 1 drink/day for women, and 2 drinks/day for men.”

- Staging in the NCCN Guidelines for Colon Cancer (ST-1)

- Global change – FLOX removed throughout the Guidelines


The following NCCN Chemotherapy Order Templates (NCCN Templates®) have been deleted to reflect the NCCN Guidelines for Colon Cancer Version 1.2018.

- COL26: FLOX (Fluorouracil/Leucovorin/OXALIplatin)

NCCN has published updates to the NCCN Radiation Therapy Compendium™ based on updates to the following NCCN Guidelines:

- Colon Cancer, Version 1.2018
- Testicular Cancer, Version 1.2018

January 17, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Testicular Cancer. These NCCN Guidelines® are currently available as Version 1.2018.

- Global Changes
AJCC Cancer Staging tables (7th edition): Following statement added, “Both the AJCC Staging for Testis Cancer 7th and 8th editions are included for reference and documentation.” (ST-1 and ST-2)

The AJCC Cancer Staging tables (8th edition) for Testis Cancer were added (ST-3, ST-4, ST-5).

Primary Treatment or a suspicious testicular mass (TEST-1)
- Sub-bullets were revised under “Consider inguinal biopsy of contralateral testis if:”
  - “Suspicious Ultrasound showing with intratesticular abnormalities mass concerning for testicular cancer.”
  - New sub-bullet added “Suspicious mass”

Pure Seminoma
- Postdiagnoistic workup (TEST-2)
  - Last bullet revised to “Discuss Recommend sperm banking, if clinically indicated.”
  - Footnote “g” regarding repeat markers was revised, “...to allow precise staging. Follow declining markers until normalization or plateau. Staging is based on marker levels at the time that the patient starts postorchiectomy therapy (for example, for patients starting chemotherapy for disseminated disease, prognostic category and staging should be assigned based on the serum tumor marker levels on day 1 of cycle 1 of chemotherapy)”
  - Footnote ”j” regarding Clinical Stage IA, IB is new: “The panel recommends using the AJCC Staging 7th edition for subclassifying and making treatment decisions about stage I tumors. (See ST-1 and ST-2)”. This footnote was also added for Nonseminoma Stages IA, IB (TEST-6)

Primary Treatment (TEST-4)
- Stage IIA: Revised to “Primary chemotherapy: BEP for 3 cycles or EP for 4 cycles for multiple positive lymph nodes”
- Stage IIC, III: Footnote “u” regarding Intermediate Risk is new: “Intermediate risk in seminoma is based on metastases to organs other than the lungs (stage IIIC). Stage IIIB does not apply to pure seminomas. Patients with elevated AFP have nonseminomas and patients with a serum bHCG above 1000 IU/L are also generally presumed to have a nonseminoma. LDH should not be used to stage or risk stratify patients with pure seminoma.”
- Stage IIA, IIB, III After Primary Treatment With Chemotherapy (TEST-5)
  - For patients with a residual mass (>3 cm) and normal serum AFP and beta-hCG, “Surveillance” was added as an option and the imaging recommendation was revised: “Consider PET/CT scan from skull base to mid-thigh (6 wks...)”

Nonseminoma
- Primary Treatment
  - Stage IB recommendations were revised: (TEST-7)
    - "Primary chemotherapy: BEP for 1–2 1 cycle"
    - "Surveillance for T2 or T3 (category 2B)"
  - Intermediate risk Stage IIIB: “VIP for 4 cycles” changed from category 2A to category 1. (TEST-11)
  - After primary treatment for Stages IS-IIIC, a new pathway was added for “Incomplete response with persistently elevated AFP and/or beta-hCG levels” followed by a new “Post-chemotherapy Management” section for this group of patients. (TEST-11)

Second-Line Therapy (TEST-12)
- For patients who received prior chemotherapy, “Recommend sperm banking if clinically indicated” was added as an option
- For patients who received no prior chemotherapy, “Discuss Recommend sperm banking if clinically indicated”

Post Second-Line Therapy (TEST-13)
A new page was added with treatment options for recurrence for patients who had received prior second-line therapy
- Third-Line Therapy (TEST-14)
  - A new third-line therapy page was added with treatment options for recurrence for patients who had received prior chemotherapy.
- Follow-up for Seminoma (TEST-A 2 of 2)
  - Table 4: The imaging time interval recommendations for "Abdominal/Pelvic CT" was revised for all years.
    - Two new footnotes were added regarding "Abdominal/Pelvic CT": "Patients with residual masses may require more frequent imaging based on clinical judgment." and "PET/CT scan skull base to mid-thigh as clinically indicated."
- Primary Chemotherapy Regimens for Germ Cell Tumors (TEST-E)
  - EP: Added "(Option only for good-risk patients [see TEST-D], patients with pathologic stage II disease, and patients with viable GCT at surgery following first-line chemotherapy)"
  - VIP: Added "(Option only for intermediate or poor-risk patients or patients with viable GCT at surgery following first-line chemotherapy (See TEST-5 and TEST-11)"
  - VIP: Mesna dose was revised.
  - New footnote "3" added for VIP, TIP, VeIP: "These regimens are high risk for febrile neutropenia and granulocyte colony-stimulating factors (G-CSF) should be used (See NCCN Guidelines for Myeloid Growth Factors)."
- Second-Line Chemotherapy Regimens for Metastatic Germ Cell Tumors (TEST-F)
  - Mesna dose revised for VeIP and TIP.
- Third-Line Chemotherapy Regimens for Metastatic Germ Cell Tumors (TEST-G)
  - Page title revised: "Subsequent Third-Line Chemotherapy Regimens For Metastatic Germ Cell Tumors"
  - Palliative Chemotherapy Regimens: "Pembrolizumab (for MSI-H/dMMR tumors)" added as an option.
- Principles of Surgery for Germ Cell Tumors (TEST-H)
  - First bullet revised, "... and post-chemotherapy setting. Referral to high-volume centers with experience in performing RPLNDs should be considered."

January 10, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Distress Management. These NCCN Guidelines® are currently available as Version 1.2018.

- Global Changes
  - Follow-up recommendation changed throughout the guidelines: "Follow-up and communication with primary oncology team, primary care physician, and family/caregivers"

- Management of Expected Distress Symptoms (DIS-5)
  - Expected Distress Symptoms: "Spiritual/existential concerns" added.
  - Interventions
    - Psychostimulants added under "Consider medication to manage symptoms"
NCCN Flash Updates™

1st Quarter 2018

- Re-evaluation: Revised, “Monitor functional level and reevaluate at each visit as appropriate”

- Distress Thermometer Problem List (DIS-A)
  - Problem List; Physical problems: “Substance abuse” changed to “Substance use”

- Psychosocial Distress Patient Characteristics (DIS-B)
  - Patients at increased risk for distress
    - Social issues: Bullet revised, “History of abuse (physical, sexual, emotional, verbal)”
    - Social issues: “Female” removed.
    - New bullet added: “Cancer type associated with risk of depression (eg, pancreatic cancer, head and neck cancer)”

- Depressive Disorders (DIS-11)
  - Treatment: For patients with “No/partial response” the following option was added “Re-evaluate psychotherapeutic intervention and consider higher level care with intensive outpatient program.” The same change was also made for Bipolar and Related Disorders (DIS-13)

- Bipolar and Related Disorders (DIS-12)
  - Under “Evaluation” a new sub-bullet was added: “Evaluate medication adherence”

- Trauma and Stressor-Related Disorders: Adjustment Disorders (DIS-18)
  - Treatment for moderate/severe adjustment disorder: For patients who are “No danger to self or others” and have “No/partial response” after medications and/or psychotherapy, “Re-evaluate psychotherapy, support, education” was added as an option.

- Social Work and Counseling Services (DIS-24)
  - “Grief and loss” was added to the list of “Practical problems”

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Primary Cutaneous B-Cell Lymphomas. These NCCN Guidelines® are currently available as Version 2.2018.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

*For your reference, the previous update (Version 1.2018) to the NCCN Guidelines for Primary Cutaneous B-Cell Lymphomas, published on November 10, 2017, is available at the following link: https://www.nccn.org/professionals/physician_gls/pdf/pcbcl.pdf

NCCN has published updates to the following NCCN Guidelines with NCCN Evidence Blocks™:

- Diffuse Large B-Cell Lymphoma, Version 7.2017
- Follicular Lymphoma, Version 7.2017
January 8, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®), and the NCCN Radiation Therapy Compendium™ for Bladder Cancer. These NCCN Guidelines® are currently available as Version 1.2018.

- **Bladder Cancer**
  - cT2 disease,
    - Primary treatment (BL-4)
      - The 2nd option was revised from, “Partial cystectomy (highly selected patients with solitary lesion in a suitable location; no Tis) and neoadjuvant cisplatin-based combination chemotherapy” to “Neoadjuvant cisplatin-based combination systemic therapy followed by partial cystectomy (highly selected patients with solitary lesion in a suitable location; no Tis).”
        - A footnote was added, “Cystectomy alone is appropriate for those not eligible to receive cisplatin-based chemotherapy.”
      - The 4th option for non-cystectomy candidates, “TURBT alone” was revised as “TURBT and consider intravesical BCG.”
    - Adjuvant treatment for non-cystectomy candidates (BL-4)
      - After no tumor, “If prior BCG, maintenance BCG” was added. (Also for BL-5.)
  - Principles of Imaging for Bladder/Urothelial Cancer, Muscle invasive (BL-A 3 of 5)
    - Abdominal and pelvic imaging, the 4th sub-bullet was revised, "Ureteroscopy if suspected upper tract lesions."
    - Suspected bone metastasis, the bullet was revised by adding, "MRI" as an option.
  - Principles of Surgical Management, Endoscopic Management of Upper Tract Urothelial Cancer (UTUC) (BL-B 4 of 4)
    - Section was added.
  - Principles of Systemic Therapy
    - The NCCN Categories of Preference has been applied to all of the suggested treatment regimens.
    - The page heading was revised by adding, "First-line chemotherapy systemic therapy for locally advanced or metastatic disease (Stage IV).” (BL-G 2 of 5)
      - The regimen options are listed under three groups, “Preferred regimens,” “Other recommended regimens,” and “Useful under certain circumstances.”
    - Subsequent systemic therapy was separated into two groups based on prior therapy and the headings were revised. (BL-G 3 of 5)
    - Subsequent systemic therapy for locally advanced or metastatic disease (Stage IV) (post-platinum)
      - The regimen options are listed under four groups, “Preferred regimen,” “Alternate preferred regimens,” “Other recommended regimens,” and “Useful under certain circumstances based on prior medical therapy.”
    - Subsequent systemic therapy for locally advanced or metastatic disease (Stage IV) (post-checkpoint inhibitor)
      - The regimen options are listed under four groups, “Preferred regimen for cisplatin ineligible, chemotherapy naïve,” “Preferred regimens for cisplatin eligible, chemotherapy naïve,” “Other recommended regimens” and “Useful under certain circumstances based on prior medical therapy.”
    - Radiosensitizing chemotherapy headings were clarified, (BL-G 4 of 5)
The first heading, “Radiosensitizing chemotherapy regimens for bladder-preserving chemoradiation following a maximal TURBT” to “Radiosensitizing chemotherapy regimens for organ-preserving chemoradiation.”

The second heading, “Radiosensitizing chemotherapy given concurrently with conventionally fractionated radiation for palliation of metastases or for pelvic recurrence after cystectomy” to “Radiosensitizing chemotherapy given concurrently with conventionally fractionated radiation for palliation of metastases or recurrence.”

The radiosensitizing regimen options are listed under two groups, “Preferred regimens” and “Other recommended regimen.”

- Principles of Radiation Management of Invasive Disease
  - A statement was added to the page, “Unless otherwise stated, doses are 1.8–2.0 Gy daily fractionation.” (BL-H 1 of 3 and BL-H 3 of 3)
  - A sub-bullet for recurrent disease was added, “Clinical target volume (CTV) should include gross disease in any suspected areas of spread at 66–74 Gy (higher dose up to 74 Gy for larger tumor and non-urothelial histology) and consideration can be given to elective regional-nodal basins (45–50.4 Gy) as discussed above, if feasible based on normal tissue constraints.” (BL-H 2 of 3)

- Upper GU Tract Tumors
  - Renal pelvis (UTT-1)
    - Primary treatment for non-metastatic disease was revised by adding “± perioperative intravesical chemotherapy” to both “Low grade” and “High grade, large, or parenchymal invasion” options.

- Primary Carcinoma of the Urethra
  - Primary treatment (PCU-3)
    - For T3, T4, palpable inguinal lymph nodes, for cN0, “± consolidative surgery” was added to “Chemoradiotherapy (preferred).”
    - For cN1/cN2, “Chemoradiotherapy followed by consideration of consolidative surgery” was revised as, “Chemoradiotherapy ± consolidative surgery.”

- Staging (ST-1)
  - The AJCC TNM Staging System Bladder Cancer was updated to the 8th edition.

NCCN has published updates to the NCCN Guidelines and the NCCN Compendium® for Penile Cancer. These NCCN Guidelines are currently available as Version 1.2018.

- Management of palpable non-bulky inguinal lymph node (PN-4)
  - For unilateral lymph node(s) <4 cm (mobile) and high-risk primary lesions, treated with ILND, the options for pN2-3 disease were revised by adding, “Pelvic lymph node dissection (PLND) ± [if pelvic nodes positive, adjuvant radiotherapy or chemotherapy (category 2B) or chemoradiotherapy (category 2B)].”
  - Footnote I was revised by adding, “Consider PET/CT scan (skull-base to mid-thigh).” (Also for PN-6 and PN-9.)

- Management of palpable bulky inguinal lymph node (PN-5)
For unilateral lymph node(s) ≥4 cm (mobile) with ≥2 nodes positive or extranodal extension after primary treatment, the options were revised by adding to PLND, “[if pelvic nodes positive, adjuvant radiotherapy] or Chemoradiotherapy (category 2B).”

Footnote r was clarified by adding, “Consider postoperative radiotherapy or chemoradiotherapy (category 2B).” (Also for PN-6.)

Principles of Radiotherapy (PN-C)
- For primary radiation/chemoradiation therapy of T1-2, N0 disease, tumor ≥4 cm, the total dose was changed from “60-70 Gy” to “65-70 Gy.”
- For primary site margin positive following penectomy, the 1st bullet for postsurgical EBRT was revised from, “60–70 Gy to the primary tumor site and surgical scar (for close margins observation may be considered)” to “If no gross disease: 45 to 60 Gy to the primary site and scar. If gross disease remains, follow guideline for T3-4, or N+.”
- Adjuvant chemotherapy, the 3rd sub-bullet was revised, “Boost gross nodes and areas of extracapsular extension to a total dose of 60 65–70 Gy.”

Principles of Chemotherapy (PN-D 2 of 3)
- Subsequent-line therapy, the 3rd bullet, 2nd sub-bullet was added, “pembrolizumab, if unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) tumor that has progressed following prior treatment and no satisfactory alternative treatment options.”

Staging (ST-1)
- The AJCC TNM Staging System for Penile Cancer was updated to the 8th edition.

January 4, 2018

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for T-Cell Lymphomas. These NCCN Guidelines® are currently available as Version 2.2018.

- The Discussion section for Extranodal NK/T-Cell Lymphoma, nasal type has been updated to reflect the changes in the algorithm. (MS-1)

*For your reference, the previous update (Version 1.2018) to the NCCN Guidelines for T-Cell Lymphomas, published on November 8, 2017, is available at the following link: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf

For the complete updated versions of the NCCN Guidelines, NCCN Guidelines with NCCN Evidence Blocks™, the NCCN Drugs & Biologics Compendium (NCCN Compendium®), the NCCN Biomarkers Compendium®, the NCCN Chemotherapy Order Templates (NCCN Templates®), the NCCN Radiation Therapy Compendium™, and the NCCN Imaging Appropriate Use Criteria (NCCN Imaging AUC™), please visit NCCN.org.
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